Corporate Presentation

August 6, 2024

Forward Looking Statements

This presentation contains forward-looking statements within the meaning of the Private Securities Litigation Reform Act of 1955 ("PSLRA") relating to, among other things, expected commercial and financial results; Rigel's ability to earn and receive milestone payments; expectations related to the potential and market opportunity of REZLIDHIA® (olutasidenib) as therapeutics for relapsed or refractory acute myeloid leukemia (AML) and other conditions; the potential and market opportunity for TAVALISSE® (fostamatinib) as therapeutics for chronic ITP and other conditions; the potential and market opportunity for GAVRETO® (pralsetinib) for the treatment of non-small cell lung cancer and advanced thyroid cancer; the regulatory approval and commercialization of fostamatinib or olutasidenib or pralsetinib in the U.S. and international markets; and Rigel's ability to further develop its clinical stage and early-stage product candidates and Rigel's partnering and collaboration/alliance efforts, including the progress of the Phase 1b clinical trial of R289 for the treatment of lower-risk myeloid dysplastic syndrome (MDS), the advancement of the Phase 2a clinical trial of R552 for the treatment of rheumatoid arthritis, and the development of olutasidenib as a therapy for a broad range of mIDH1+ cancers, including but not limited to AML, MDS, and glioma, and Rigel's partnering efforts and ability to achieve regulatory and commercial milestones and earn and receive milestone payments.

Any statements contained in this presentation that are not statements of historical fact may be deemed to be forward-looking statements and as such are intended to be covered by the safe harbor for "forward-looking statements" provided by the PSLRA. Forward-looking statements can be identified by words such as "plan", "potential", "may", "expects", "will" and similar expressions in reference to future periods. Forward-looking statements are neither historical facts nor assurances of future performance. Instead, they are based on Rigel's current beliefs, expectations, and assumptions and hence they inherently involve significant risks, uncertainties and changes in circumstances that are difficult to predict and many of which are outside of Rigel's control. Therefore, you should not rely on any of these forward-looking statements. Actual results and the timing of events could differ materially from those anticipated in such forward looking statements as a result of these risks and uncertainties, which include, without limitation, risks and uncertainties associated with the commercialization and marketing of fostamatinib, olutasidenib or pralsetinib; risks that the FDA, European Medicines Agency, PMDA or other regulatory authorities may make adverse decisions regarding fostamatinib, olutasidenib or pralsetinib; risks that clinical trials may not be predictive of real-world results or of results in subsequent clinical trials; risks that fostamatinib, olutasidenib or pralsetinib may have unintended side effects, adverse reactions or incidents of misuses; the availability of resources to develop, manufacture and commercialize Rigel's product candidates; market competition; and those other risks detailed from time to time in Rigel's reports filed with the Securities and Exchange Commission, including its Annual Report on Form 10-K for the year ended December 31, 2023 and subsequent filings. Any forward-looking statement made by us in this press release is based only on information currently available to us and speaks only as of the date on which it is made. Rigel does not undertake any obligation to update forward-looking statements, whether written or oral, that may be made from time to time, whether as a result of new information, future developments or otherwise, and expressly disclaims any obligation or undertaking to release publicly any updates or revisions to any forward-looking statements contained herein, except as required by law.

Growing Our Hematology and Oncology Business

Commercial Execution

Tavalisse® (fostamatinib disodium hexahydrate) tablets

ITP

REZLIDHIA® (olutasidenib) 150 mg capsules

m*IDH1* R/R AML

GAVRETO® pralsetinib 100mg capsules

RET fusion-positive NSCLC or TC

Development & Expansion

Development Programs[1]

- Evaluate REZLIDHIA in a broad range of *IDH1*-mutant cancers including AML, MDS and glioma
- Complete enrollment of R289, IRAK1/4 inhibitor, Phase 1b trial in lower-risk MDS

In-Licensing and Product Acquisition

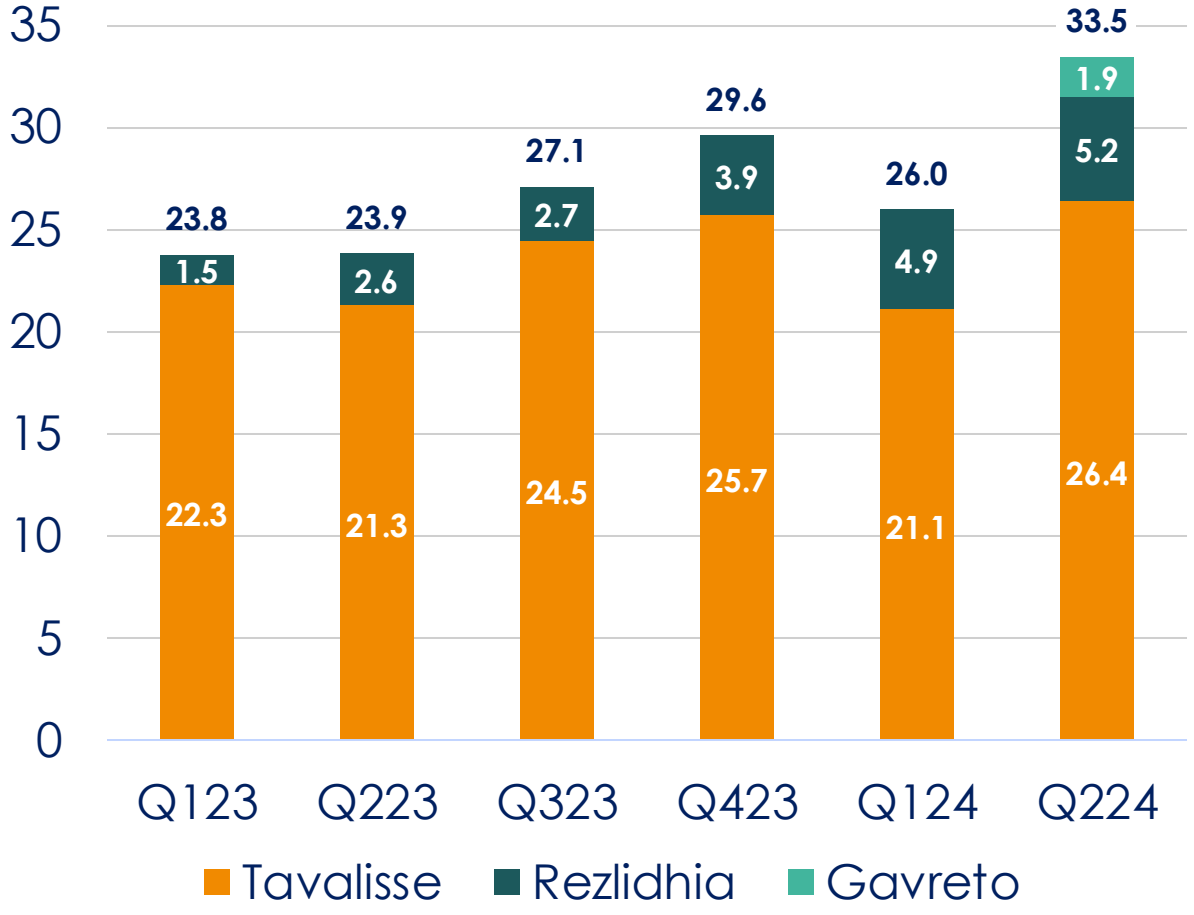
- Identify new late-stage assets which leverage current capabilities and capacity

Financial Discipline

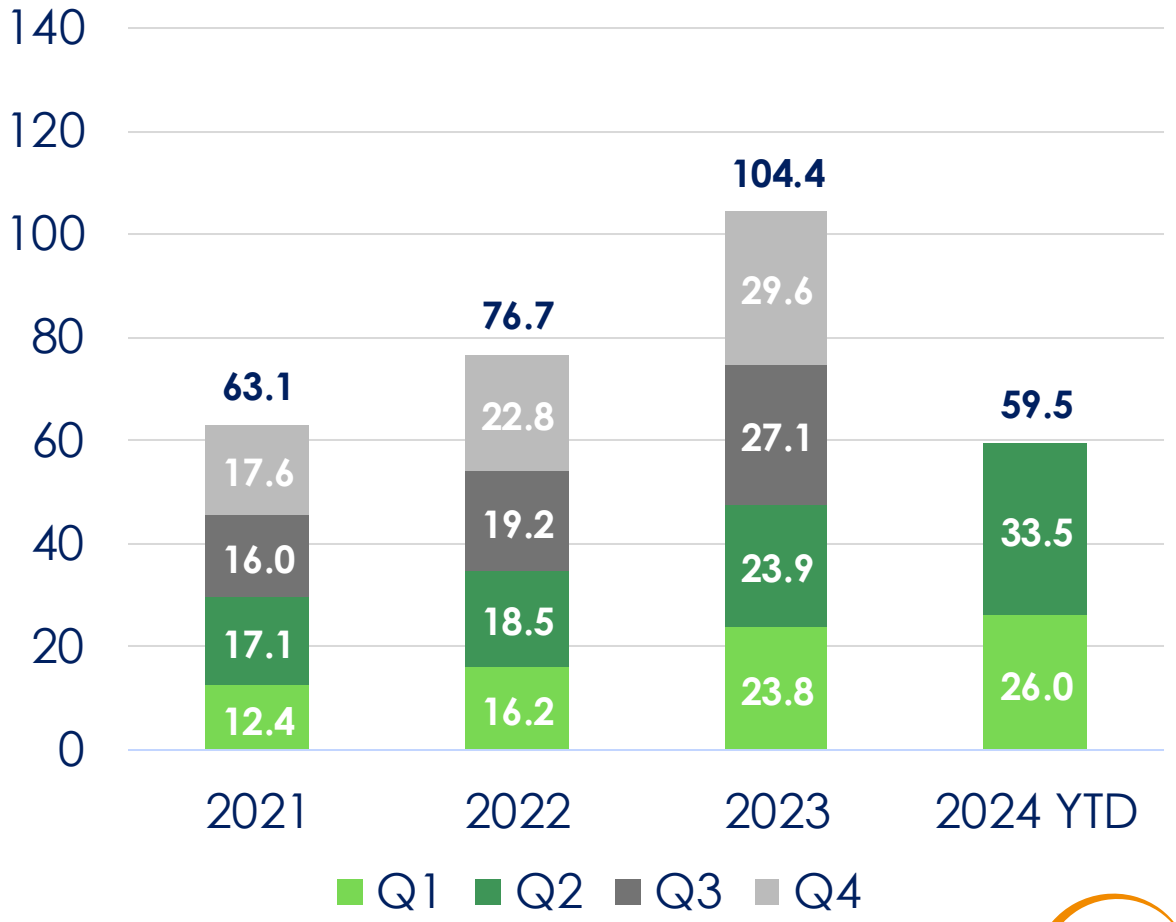
ITP, immune thrombocytopenia; IDH1, isocitrate dehydrogenase-1; m*IDH1*, mutated IDH1; R/R, relapsed or refractory; AML, acute myeloid leukemia; RET, rearranged during transfection; NSCLC, non-small cell lung cancer; TC, thyroid cancer; MDS, myelodysplastic syndrome; IRAK1/4, interleukin receptor-associated kinases 1 and 4. **1.** Investigational compounds in these indications and not approved by the FDA. Please see Important Safety Information on slides 44-48. Please visit www.TAVALISSE.com for Full Prescribing Information. Please visit www.REZLIDHIA.com for Full Prescribing Information, including Boxed WARNING. Please visit www.GAVRETO.com for Full Prescribing Information.

US Net Product Sales Growth

Quarterly Net Product Sales ($M)



Annual Net Portfolio Sales ($M)



Grow Sales of TAVALISSE in ITP

Tavalisse®
(fostamatinib disodium hexahydrate) tablets

Kinase inhibitor indicated for the treatment of thrombocytopenia in adult patients with chronic immune thrombocytopenia (cITP) who have had an insufficient response to a previous treatment.

Select Important Safety Information

Adverse Reactions:

- Serious adverse drug reactions in the ITP double-blind studies were febrile neutropenia, diarrhea, pneumonia, and hypertensive crisis, which occurred in 1% of TAVALISSE patients. In addition, severe adverse reactions occurred including dyspnea and hypertension (both 2%), neutropenia, arthralgia, chest pain, diarrhea, dizziness, nephrolithiasis, pain in extremity, toothache, syncope, and hypoxia (all 1%).
- Common adverse reactions (≥5% and more common than placebo) from FIT-1 and FIT-2 included: diarrhea, hypertension, nausea, dizziness, ALT and AST increased, respiratory infection, rash, abdominal pain, fatigue, chest pain, and neutropenia.

Please see Important Safety Information on slide 44. Please visit www.TAVALISSE.com for Full Prescribing Information.

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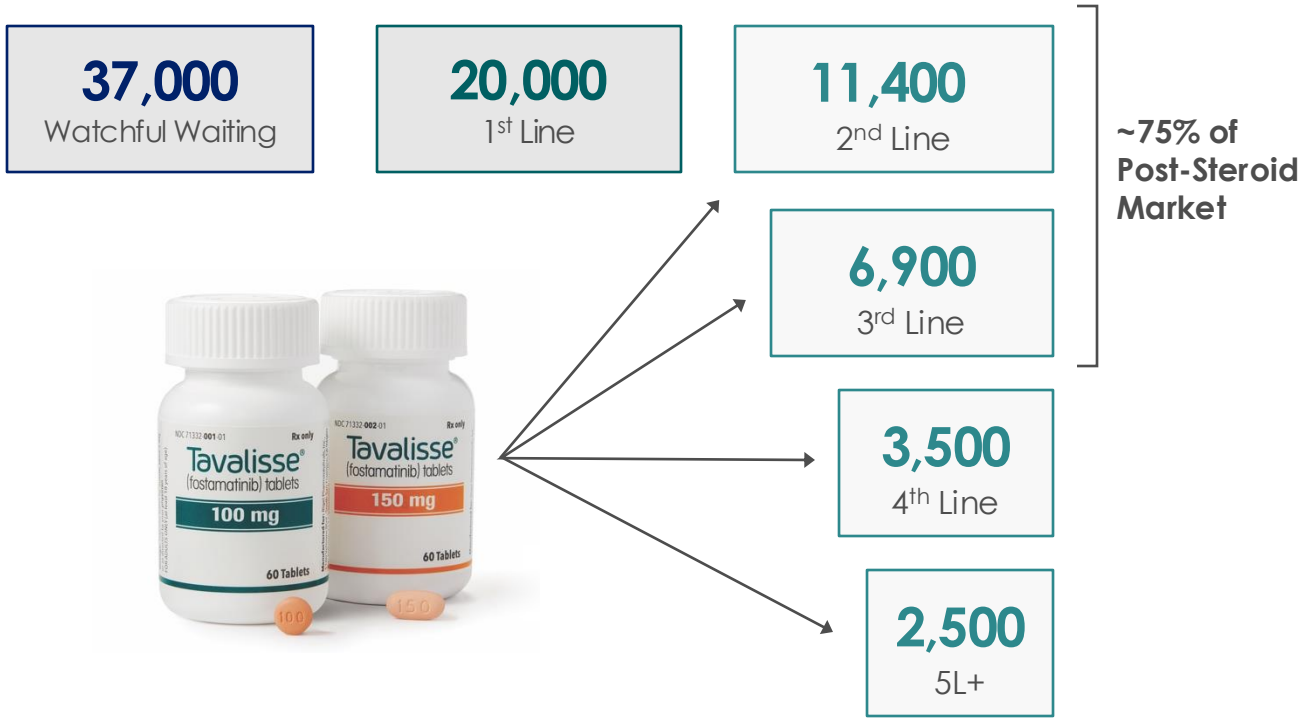
Creating Opportunities to Gain Market Share

Tavalisse (fostamatinib disodium hexahydrate) tablets

81,300 U.S. Adult cITP Patients[1]



44,300 Patients Actively Treated[2]

- 24,300 patients are 2L or later

Patient Moving through Therapies Creates New Patient Opportunities

TAVALISSE is Now Preferred on Key Commercial National Formularies

- Significant national commercial coverage
- Reinforces TAVALISSE's proven efficacy and safety
- Strengthens reimbursement confidence
- Spreading awareness among customers through personal and non-personal channels

cITP, chronic immune thrombocytopenia. **1.** Symphony Health, PatientSource®, 10 years ending September 2019; **2.** Internal market research conducted in October 2020.
Please see Important Safety Information on slide 44. Please visit www.TAVALISSE.com for full prescribing information.

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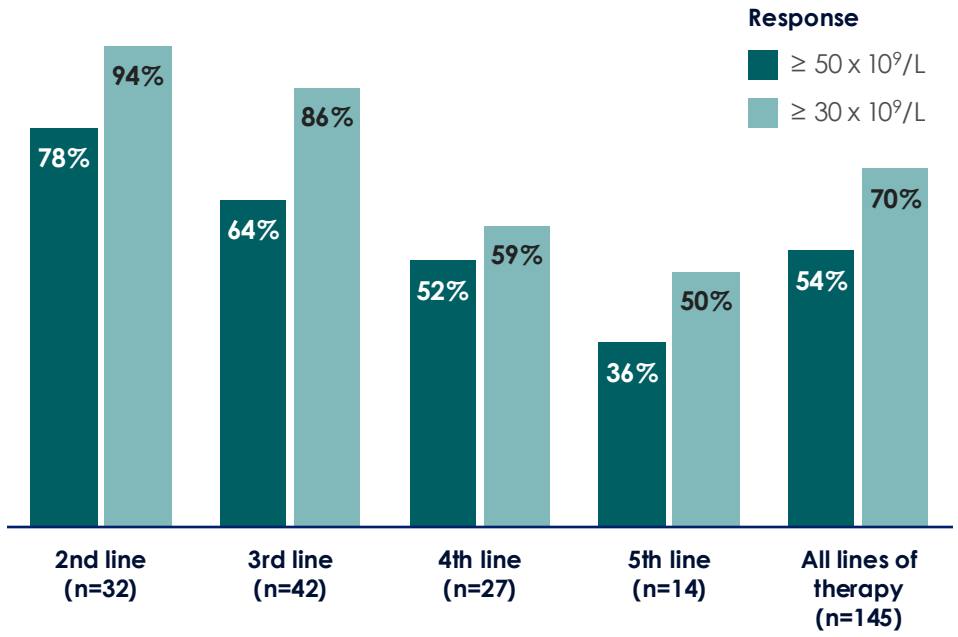
Promotion Efforts Highlight Data Supporting Use in Earlier Lines

Tavalisse® (fostamatinib disodium hexahydrate) tablets

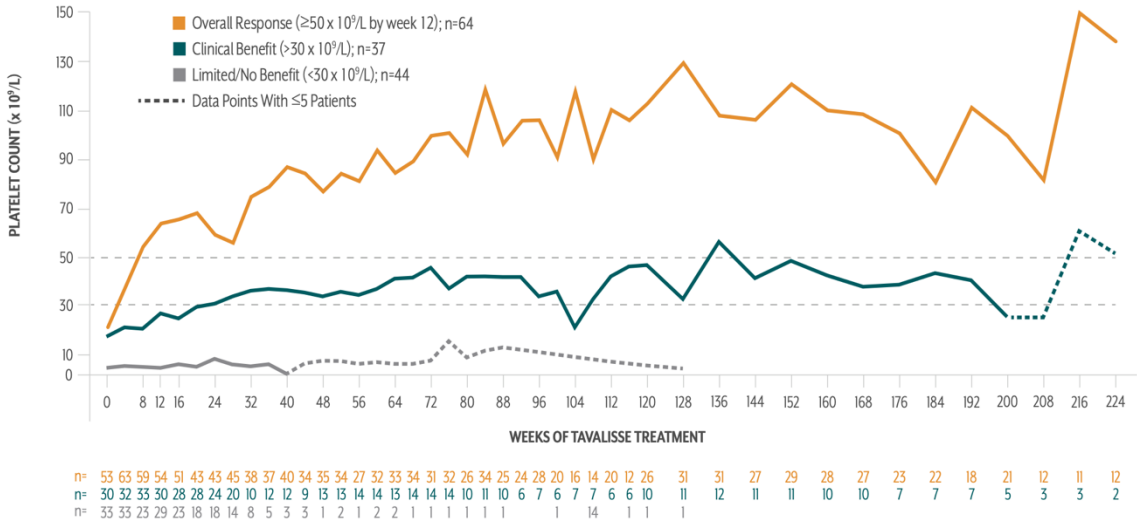
Post-hoc Data Analysis Demonstrated Use as 2nd-Line Therapy Resulted in Higher Response Rates[1,2]



Durable Efficacy was Observed in Responders to TAVALISSE in the FIT Studies

(combined results from FIT-1, FIT-2, and FIT-3)[3]

Median Platelet Counts Over Time



FIT, Fostamatinib in ITP

1. Fostamatinib is an effective 2nd-line therapy in patients with immune thrombocytopenia, British Journal of Haematology. **2.** Percentage of Patients Achieving Target Platelet Counts at Any Visit. **3.** Assessment of thrombotic risk during long-term treatment of immune thrombocytopenia with fostamatinib, Therapeutic Advances in Hematology, 4/30/21. Please see Important Safety Information on slide 44. Please visit www.TAVALISSE.com for Full Prescribing Information.

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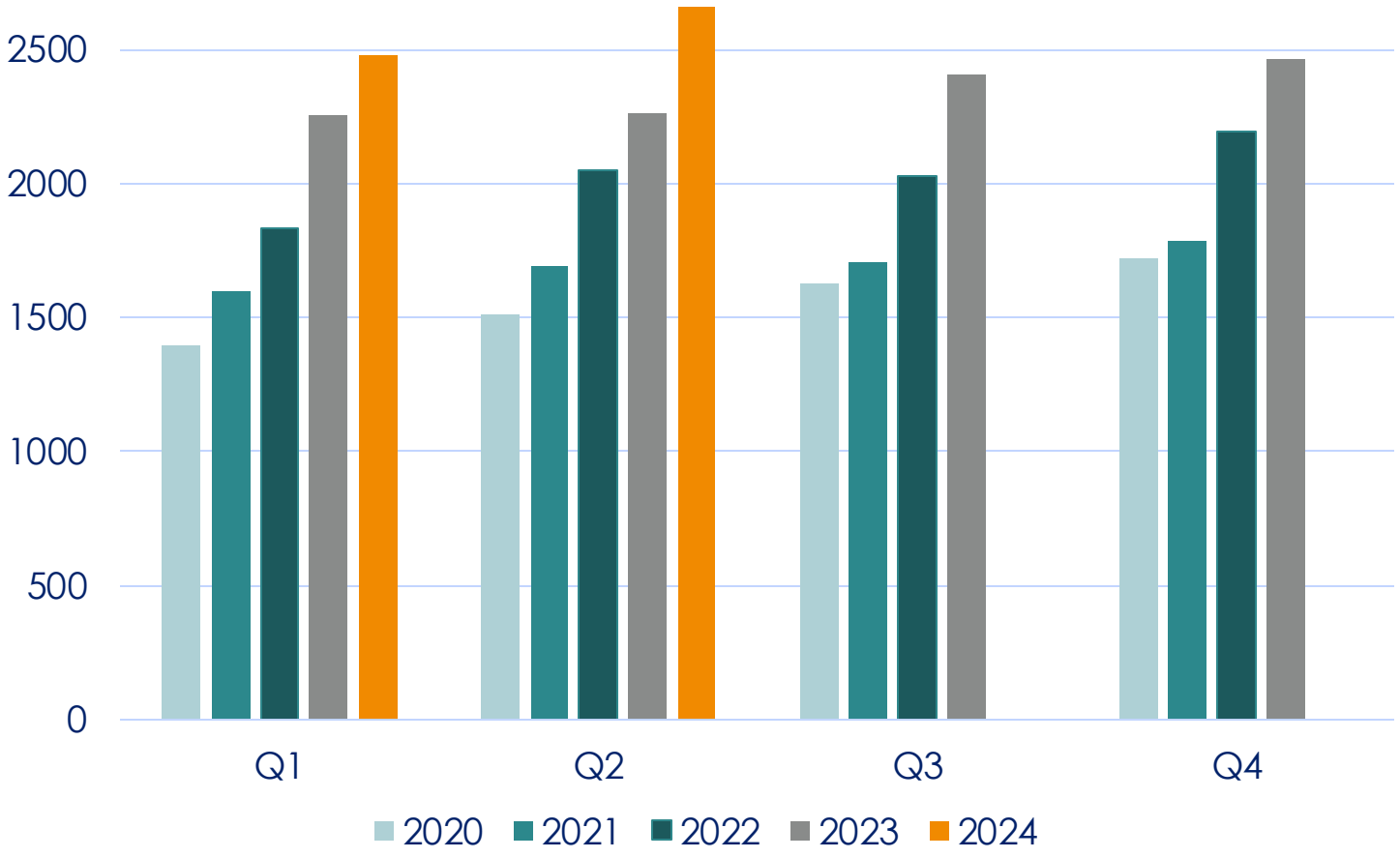
TAVALISSE Q2 2024 Performance

Tavalisse® (fostamatinib disodium hexahydrate) tablets

Bottles Shipped to Patients and Clinics



$26.4M Q2 2024 Net Product Sales

24% Growth vs. Q1 2024

25% Growth vs. Q2 2023

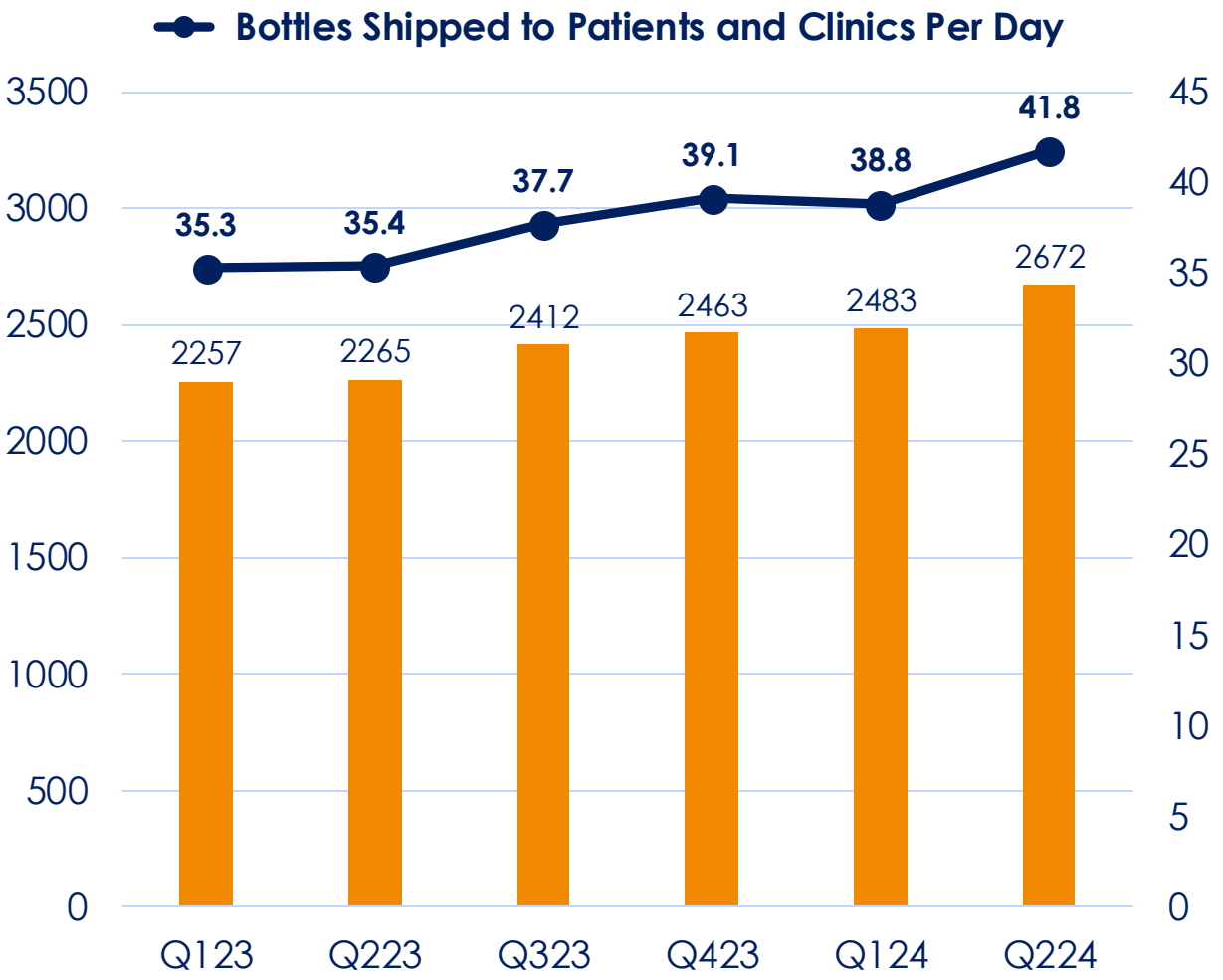
2,672 Bottles Shipped to Patients and Clinics in Q2 2024

8% Growth vs. Q1 2024

18% Growth vs. Q2 2023

TAVALISSE Q2 2024 Sales Growth

Tavalisse® (fostamatinib disodium hexahydrate) tablets



Sales Growth Accelerated in Q2

- Growth of 3 bottles shipped per day over Q1 is the largest increase in 2 years
- Bottles shipped per day consistently increased throughout each month of Q2
- Continuous flow of new patient starts and carryover from refills driving stronger growth in 2024

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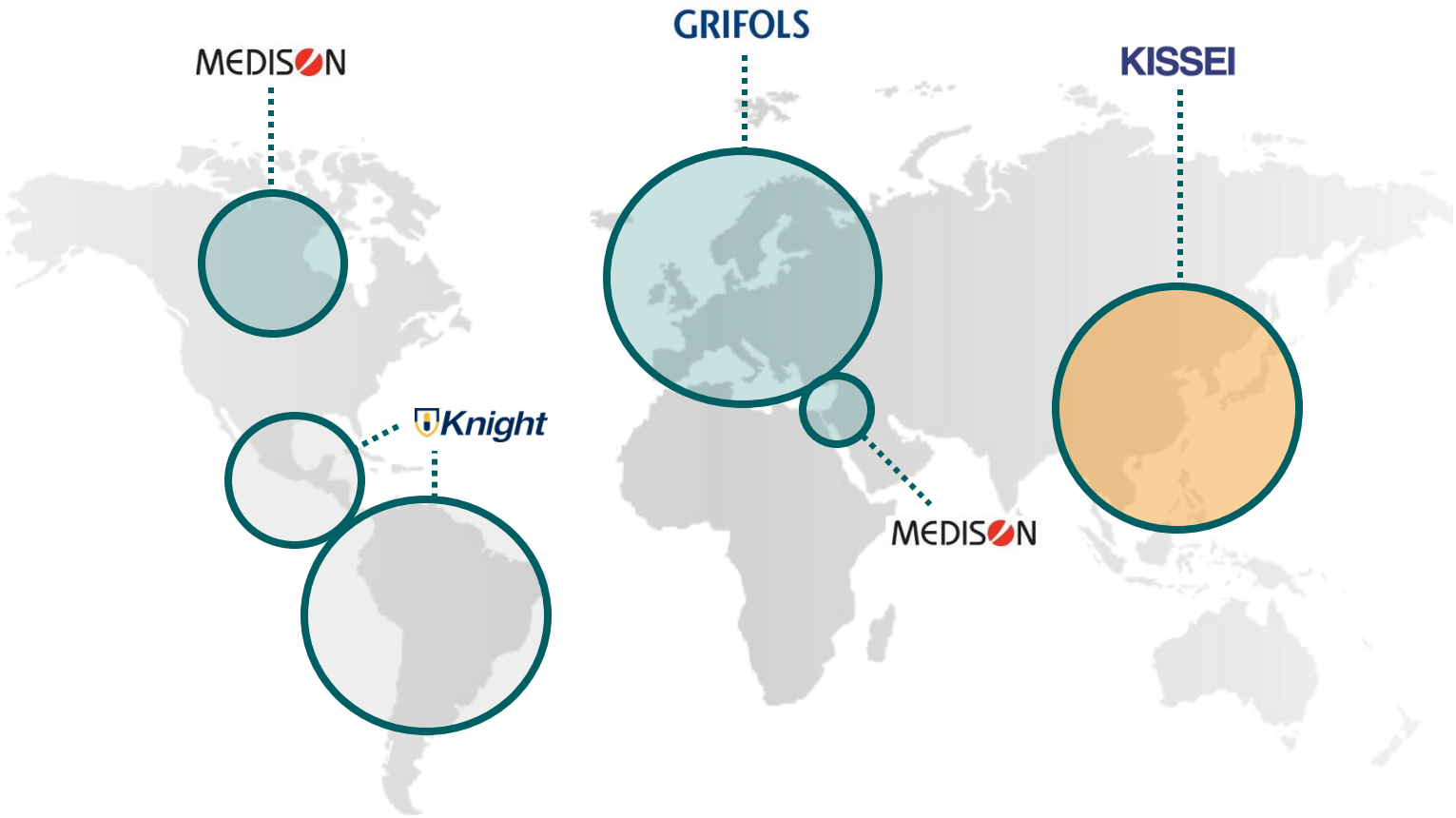
Expanding Access in Global Markets

Tavalisse (fostamatinib disodium hexahydrate) tablets



- In April 2023, Kissei launched TAVALISSE in Japan for the treatment of chronic ITP

- TAVALISSE is also commercially available in key European countries (TAVLESSE), Canada and Israel

ITP, immune thrombocytopenia

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Grow Sales of REZLIDHIA in m*IDH1* R/R AML

REZLIDHIA®
(olutasidenib) 150 mg capsules

APPROVED AND AVAILABLE IN THE U.S.

REZLIDHIA is indicated for the treatment of adult patients with relapsed or refractory acute myeloid leukemia (AML) with a susceptible IDH1 mutation as detected by an FDA-approved test.

Please see Important Safety Information on slides 45 & 46, including Boxed WARNING regarding differentiation syndrome

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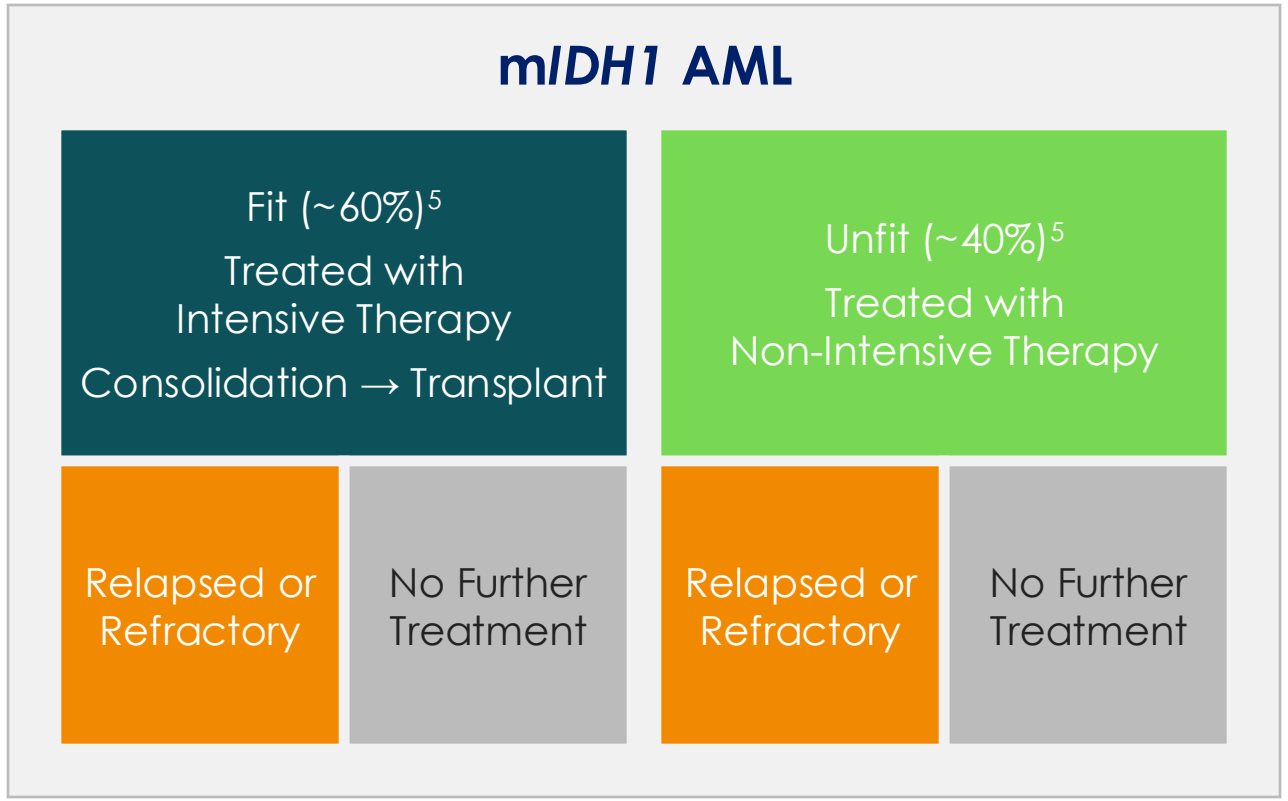
m*IDH1* Relapsed/Refractory AML Background

REZLIDHIA® (olutasidenib) 150 mg capsules

- AML is an aggressive, highly complex malignancy typically diagnosed in older adults[1]
- AML will be diagnosed in over 20K patients and result in nearly 11.2K deaths in 2024[2]
- IDH1 mutations are found in 6-9%[3,4] of AML
- m*IDH1* patients are well-identified, and have limited options for treatment, particularly in relapsed/refractory (R/R) disease
- A significant unmet need exists for targeted treatments for m*IDH1* R/R AML that are well-tolerated and efficacious



IDH1, isocitrate dehydrogenase-1; m*IDH1*, mutated IDH1; R/R, relapsed or refractory; AML, acute myeloid leukemia.

1. Leukemia & Lymphoma Society, Facts About Acute Myeloid Leukemia (AML), December 2019. **2.** American Cancer Society, Key Statistics for Acute Myeloid Leukemia (AML), 2024.
3. Abbas S et al. Acquired mutations in the genes encoding IDH1 and IDH2 both are recurrent aberrations in acute myeloid leukemia: prevalence and prognostic value. Blood (2010) 116 (12): 2122-2126.
4. Chotirat S et al. Molecular alterations of isocitrate dehydrogenase 1 and 2 (IDH1 and IDH2) metabolic genes and additional genetic mutations in newly diagnosed acute myeloid leukemia patients. J Hematol Oncol 5, 5 (2012). **5.** Rigel HCP Quantitative Market Research, 2022 (Data on File).

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REZLIDHIA Phase 2 Clinical Trial: Study Design[1]

REZLIDHIA (olutasidenib) 150 mg capsules

Monotherapy

REZLIDHIA[2] 150 mg BID

- **Cohort 1:** R/R AML (N=153)
- **Cohort 2:** AML in CR/CRi but MRD positive
- **Cohort 3:** R/R AML/MDS treated previously with IDH1 inhibitor therapy AND standard treatments are contraindicated
- **Cohort 7:** TN AML for whom standard treatments are contraindicated

Combination Therapy

REZLIDHIA[2] 150 mg BID + AZA[3]

- **Cohort 4:** R/R AML/MDS naïve to prior HMA and IDH1 inhibitor therapy
- **Cohort 5:** R/R AML/MDS inadequately responded to or progressed on prior HMA
- **Cohort 6:** R/R AML/MDS treated previously with IDH1 inhibitor monotherapy as last prior therapy
- **Cohort 8:** TN AML candidates for AZA as first-line treatment

Primary Endpoint:

- CR+CRh rate

Key Secondary Endpoints:

- ORR, DOR, Transfusion independence, OS
- Safety

Cohort 1: All adults, median age 71 (32-87) years, 73% had intermediate AML cytogenetic risk. Most (75%) had ≥1 co-occurring mutations. Most (97%) had prior induction therapy and a median 2 (1-7) prior treatments (all naïve to m1DHI-inhibitor).

IDH1, isocitrate dehydrogenase-1; m*IDH1*, mutated IDH1; R/R, relapsed or refractory; AML, acute myeloid leukemia; BID, twice daily; CR, complete remission; CRh, CR with partial hematologic recovery; CRi, CR with incomplete count recovery; MRD; minimal residual disease; HMA, hypomethylating agents; ORR, overall response rate; DOR, duration of response, OS, overall survival; AZA, azacitidine.
1. NCT02719574. **2.** REZLIDHIA PO given daily over continuous 28-day cycles. **3.** AZA IV or SC given daily on Days 1–7 of each 28-day cycle; patients received first dose >6 months prior to data cutoff of June 18, 2021. Source: Journal of Clinical Oncology 39, no. 15_suppl (May 20, 2021) 7006-7006 doi: 10.1200/JCO.2021.39.15_suppl.7006

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REZLIDHIA Phase 2 Clinical Trial: Summary

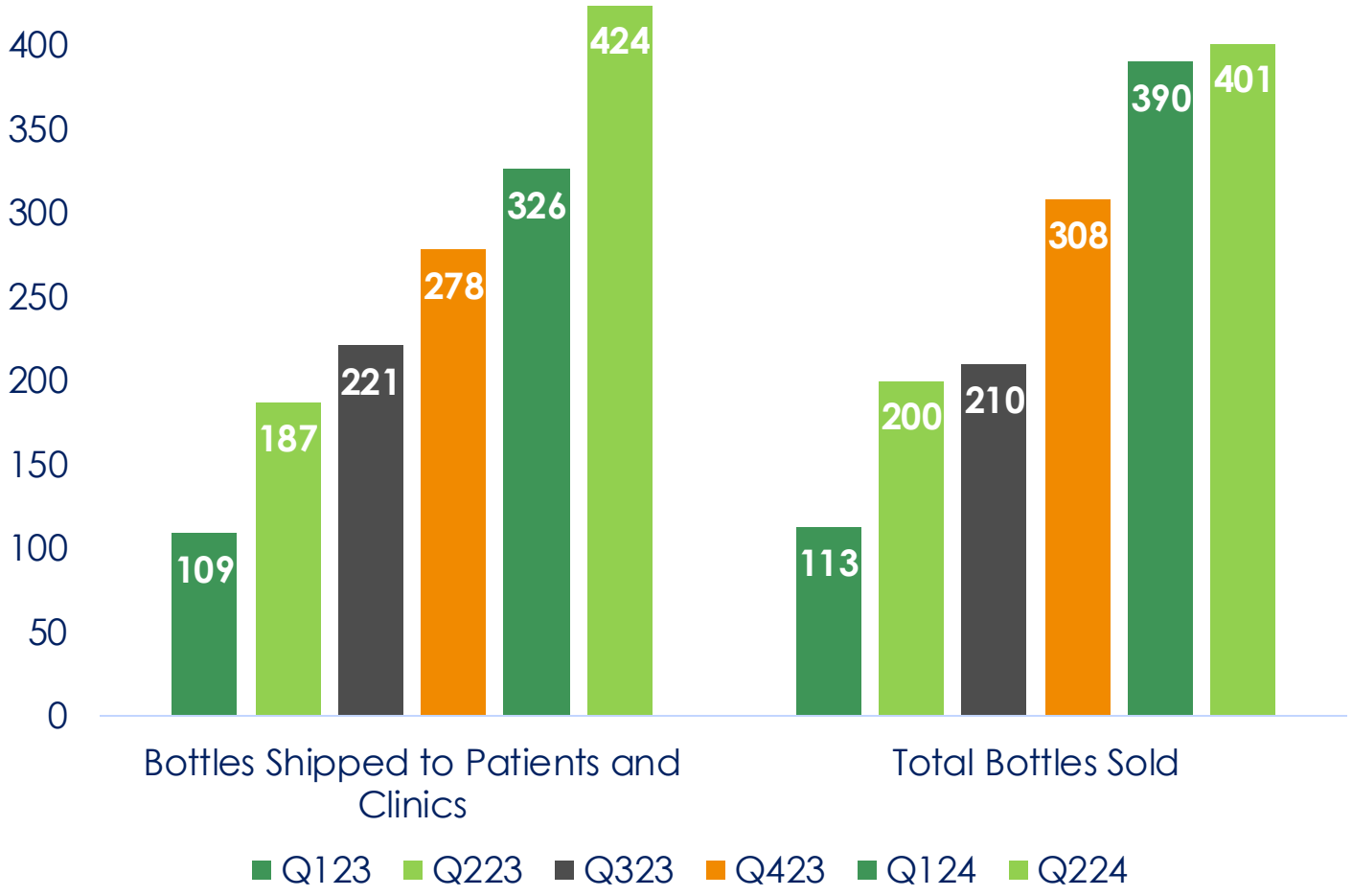
- CR+CRh rate of 35%, with a median duration of response of 25.9 months
- 92% of CR+CRh responders were CR, with a median duration of response of 28.1 months
- Transfusion independence was achieved in all subgroups
- REZLIDHIA has a well characterized safety profile with no cardiac events leading to discontinuation

CR, complete remission; CRh, CR with partial hematologic recovery

REZLIDHIA Q2 2024 Performance

REZLIDHIA® (olutasidenib) 150 mg capsules

Rezlidhia Sales



424 Bottles Shipped to Patients and Clinics in Q2 2024

30% vs. Q1 2024

127% vs. Q2 2023

$5.2M Q2 2024 Net Product Sales

5% vs. Q1 2024

102% vs. Q2 2023

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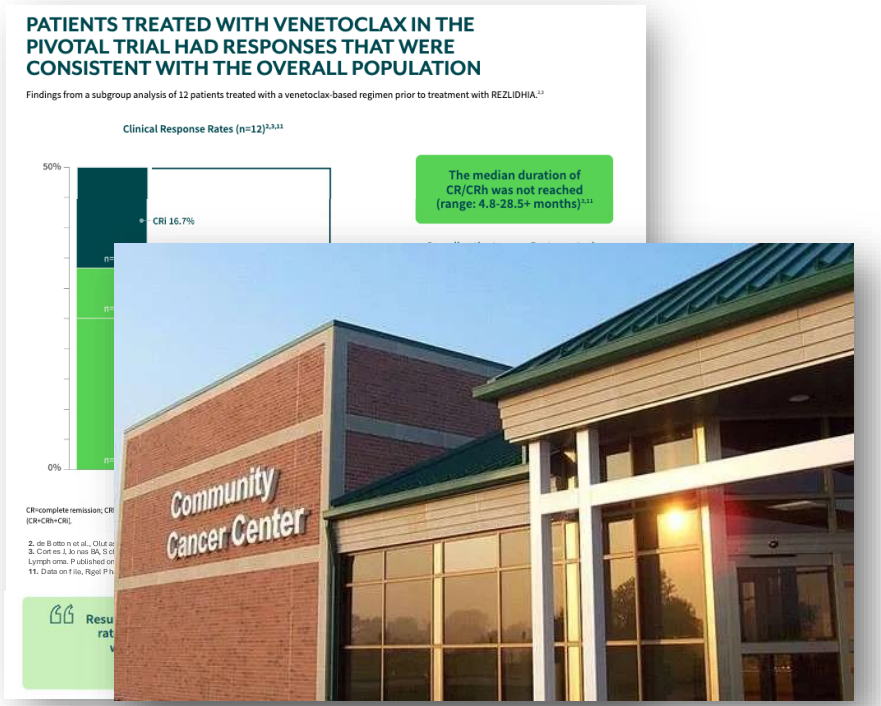
REZLIDHIA Q2 2024 Sales Growth

REZLIDHIA® (olutasidenib) 150 mg capsules

Growing Community Usage



Q2 2024 Growth Drivers

- Community volume represented nearly 25% of sales in Q2, representing strong growth vs. Q1
- Awareness and support continues to grow, as more clinicians are finding the post-venetoclax data clinically relevant
- Significant opportunity remains to improve adoption in relapsed/refractory m*IDH1* AML

mIDH1, mutated IDH1; IDH1, isocitrate dehydrogenase-1; AML, acute myeloid leukemia.

Please see Important Safety Information on slides 45 & 46. Please visit www.REZLIDHIA.com for Full Prescribing Information, including Boxed WARNING.

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GAVRETO in RET Fusion-Positive NSCLC or Thyroid Cancer

GAVRETO®

pralsetinib | 100 mg capsules

APPROVED IN THE U.S.

GAVRETO is indicated for the treatment of adult patients with metastatic rearranged during transfection (RET) fusion-positive non-small cell lung cancer as detected by an FDA-approved test, and adult and pediatric patients 12 years of age and older with advanced or metastatic RET fusion-positive thyroid cancer who require systemic therapy and who are radioactive iodine-refractory (if radioactive iodine is appropriate)*

Please see Important Safety Information on slides 47 & 48

* This indication is approved under accelerated approval based on overall response rate and duration of response. Continued approval for this indication may be contingent upon verification and description of clinical benefit in confirmatory trial(s).

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Acquired U.S. Rights to GAVRETO®

GAVRETO (pralsetinib) is a once daily, small molecule, oral, kinase inhibitor of wild-type RET (rearranged during transfection) and oncogenic RET fusions

Highly synergistic with Rigel's current product portfolio and existing commercial infrastructure and expertise

Generated **~$28M** in U.S. net product sales in 2023[1]

Patents that have issued or are expected to issue covering GAVRETO will have statutory expiration dates between 2036 and 2041

- **Established U.S. marketed product**
- Blueprint will receive a purchase price of **$15.0M**
  - **$10.0M** payable upon first commercial sale by Rigel (paid in July 2024)
  - **$5.0M** payable on the first anniversary of the closing date, subject to certain conditions
- Blueprint is also eligible to receive up to $97.5M in future commercial milestone payments and up to $5.0M in future regulatory milestone payments, in addition to tiered royalties ranging from 10% to 30%

RET, rearranged during transfection.

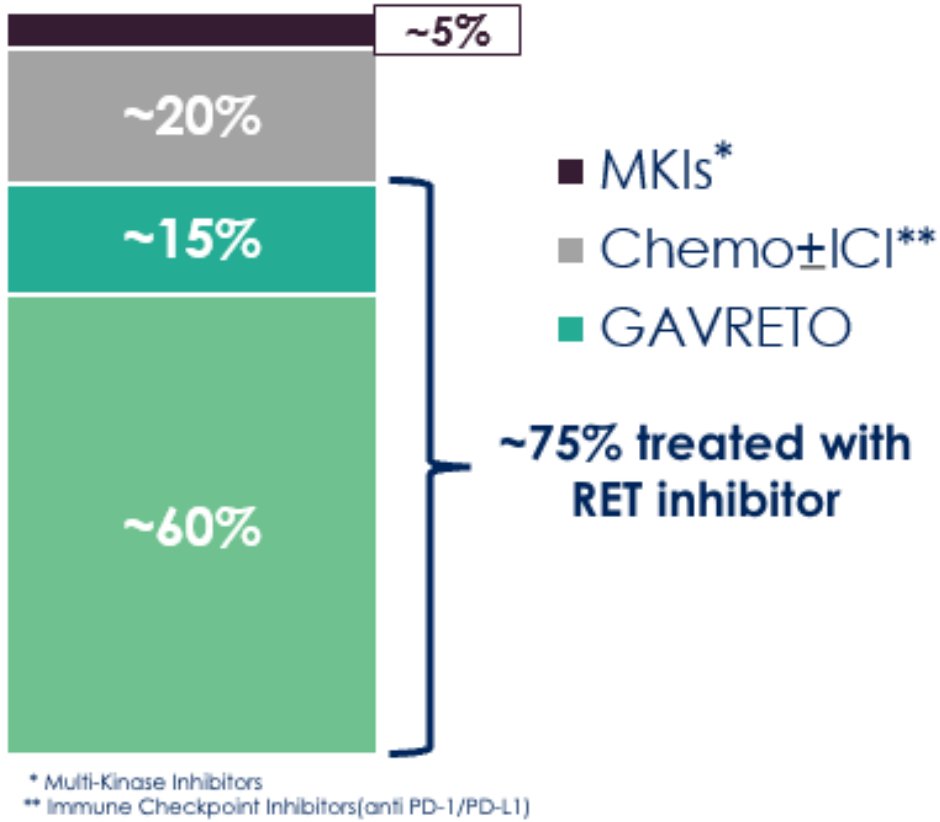
1. U.S. Net sales provided by Blueprint Medicines as reported by Genentech, a member of the Roche group. Please see Important Safety Information on slides 47 & 48. Please visit www.GAVRETO.com for Full Prescribing information.

Growing Our Oncology Targeted Therapy Portfolio

A Compelling and Synergistic Opportunity

- Enables entry into a well-identified subset of large solid tumor market
  - Immediately recognizable population of RET fusion-positive patients
  - Challenging to treat with platinum-based chemotherapy and checkpoint inhibitors
- Leverages patient access
  - Efficient product distribution
  - Responsive Rigel ONECARE patient services
  - Strong coverage and reimbursement
- Complementary to our field capabilities
  - Commercial and Medical Affairs teams in both academic and community settings

1L Treatment of RET fusion-positive NSCLC Patients[1]



RET, rearranged during transfection; NSCLC, non-small cell lung cancer. **1.** Market Research conducted in Q2 2023 with 60 oncologists managing RET fusion-positive patients.

Biomarker-Based Therapy is Standard of Care for NSCLC

RET-fusion positive cancers

- RET fusions are present in ~2% of NSCLC[1,2], the most common type of lung cancer, and ~20% of papillary thyroid cancers[3]
- Testing for RET is an essential part of the pre-treatment evaluation of NSCLC
- Practice guidelines recommend targeted therapies as first-line treatment for eligible patients with metastatic NSCLC who have actionable genetic variants such as RET fusions

RET-fusion positive NSCLC

Suboptimal responses with platinum-based regimens (ORR ~50%; median PFS: 6-8m)[4]

Inferior outcomes with non-selective multi-kinase inhibitors (ORR <30%)[5-9]

Low PD-L1 expression so immune checkpoint inhibitors are less effective (ORR <10%)[10]

Pralsetinib is an oral highly potent, selective RET inhibitor dosed once daily that is FDA-approved for RET fusion-positive NSCLC or thyroid cancer* (first line or subsequent therapy)

* This indication is approved under accelerated approval based on overall response rate and duration of response. Continued approval for this indication may be contingent upon verification and description of clinical benefit in confirmatory trial(s).

NSCLC, non-small cell lung cancer; RET, rearranged during transfection; ORR, overall response rate.

1. Lipson, et al. Nat Med 2012 **2.** Takeuchi, et al. Nat Med 2012 **3.** Santoro, et al. J Clin Invest 1992 **4.** Gautschi O, et al.J Clin Oncol. 2017. **5.** Drilon A et al. *Nat Rev Clin Oncol* 2018. **6.** Lee SH et al. *Annals of Oncology*. 2017. **7.** Drilon A et al. *Lancet Oncology*. 2016. **8.** Hida T et al. *Lung Cancer*. 2019. **9.** Horiike A et al. *Lung Cancer*. 2016. **10.** Mazieres J, et al. J Clin Oncol 2018;36(15 suppl)

Pralsetinib in RET Fusion + Solid Tumors: Updated Results from the Phase 1/2 "ARROW" Study

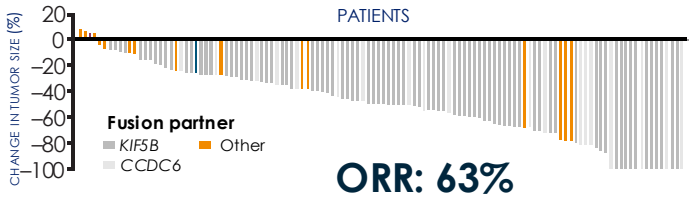
Potential for better response rates when used first-line in NSCLC[1]

Phase 1:
Dose Escalation
Pralsetinib 30-600 mg QD or BID

Phase 2
RP2D: 400 mg QD

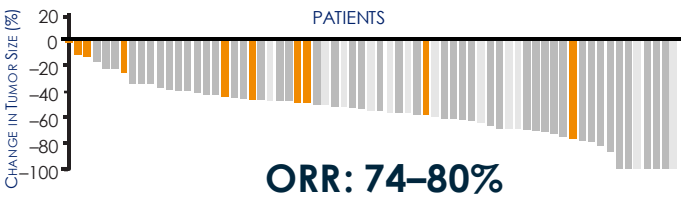
RET fusion+ NSCLC (n=260)

Prior platinum treatment (n=130)



ORR: 63%

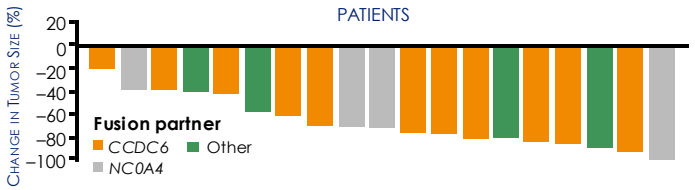
Treatment-naïve (n=107)



ORR: 74–80%

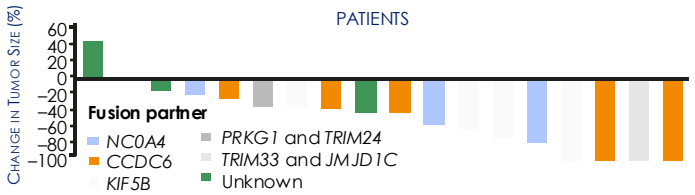
Median duration of response: 19.1 months (14.5-27.3)[1] (all NSCLC)

RET fusion+ TC (n=22)



ORR: 91%

Other RET fusion+ solid tumors* (n=23)
*** Investigational use**



ORR: 57%

QD, once daily; BID, twice daily dosing; RP2D, recommended phase 2 dose; TC, thyroid cancer; ORR, overall response rate; NSCLC, non-small cell lung cancer; RET, rearranged during transfection.

1. Besse B et al. Ann Oncol. 2022; 33(suppl 7)

Promising Intracranial Efficacy in NSCLC Patients with Brain Metastases – ARROW Study[1]

25% of RET fusion-positive NSCLC patients have brain metastases at diagnosis[2]

Intracranial response in patients with measurable CNS metastases at baseline (n=15)[1]

	N=15
CNS ORR, % (95% CI)	**53.3** (26.6–78.7)
CR, n (%)	**3** (20.0)
PR, n (%)	5 (33.3)
	n=8
Median DOR, months (95% CI)[a]	**11.5** (9.2–NR)
Median follow-up, months (95% CI)	29.7 (24.1–35.3)

[a]Per EMA censoring rule.
CI, confidence interval; CNS, central nervous system; CR, complete response; DOR, duration of response; NSCLC, non-small cell lung cancer; PR, partial response, ORR, overall response rate; RET, rearranged during transfection.

1. Besse B et al. Ann Oncol. 2022; 33(suppl 7) **2.** Drilon A,. J Thorac Oncol 2018;13

Pralsetinib Has a Differentiated Value Proposition

The **only once daily, oral,** RET inhibitor approved for patients with NSCLC and thyroid cancer with RET gene fusions

High and durable response rates regardless of prior treatment history[1]

Promising intracranial efficacy in patients with **brain metastases**[1]

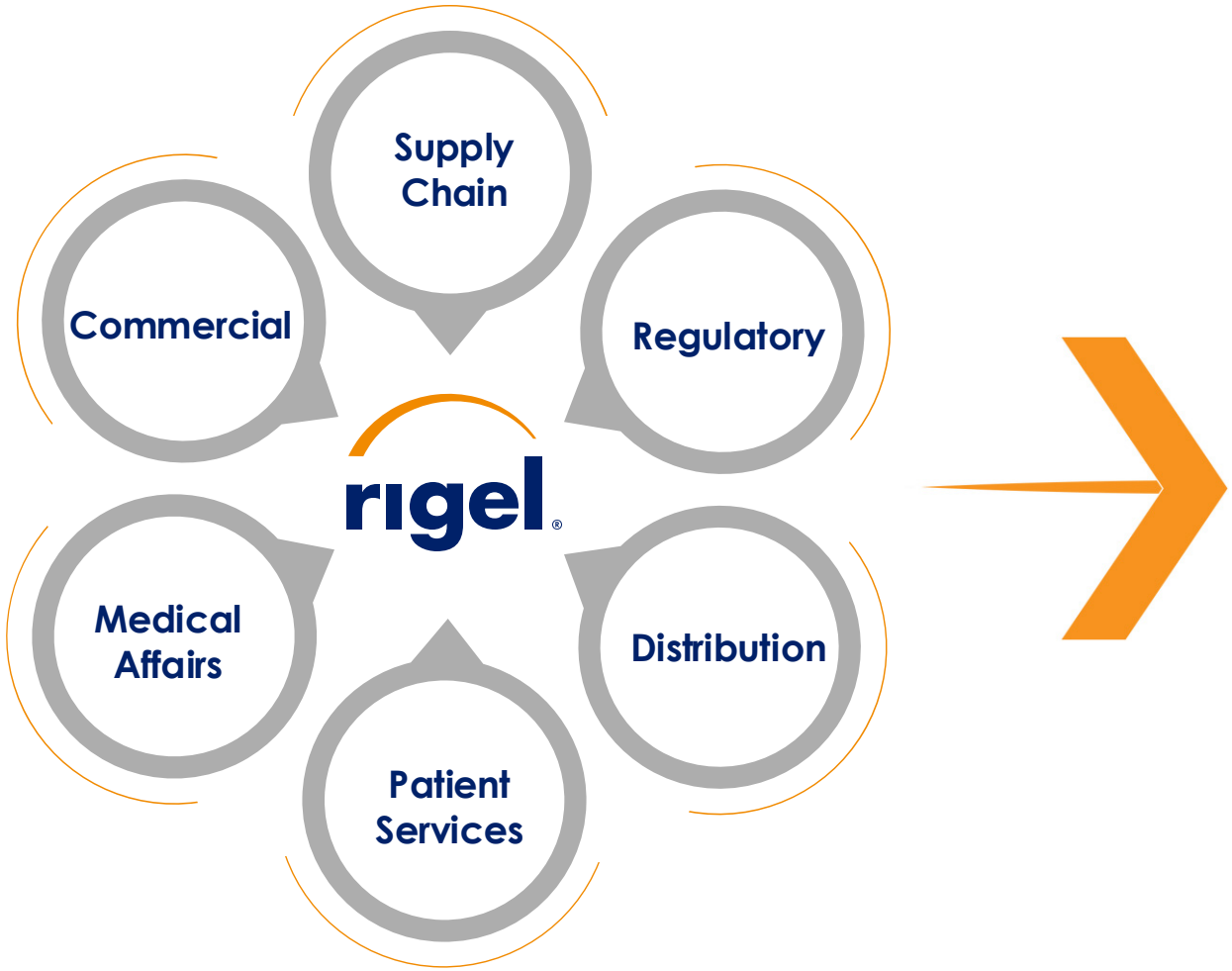
Established **safety and tolerability** profile

Practice guidelines **recommended treatment option for patients with RET+ mNSCLC and advanced thyroid cancer**

MNSCLC, metastatic non-small cell lung cancer; NSCLC, non-small cell lung cancer; RET, rearranged during transfection

1. Besse B et al. Ann Oncol. 2022; 33(suppl 7) Please visit www.GAVRETO.com for Full Prescribing information.

GAVRETO Stocked and Now Shipping



Smooth Transition Under Way

- 3PL shipments to distributors began on June 27th
- Product stocked in Rigel distribution network on June 28th, **ahead of July 1st target**
- Distribution network began shipping **GAVRETO** bottles to patients and clinics on July 1st

GAVRETO Transition Plan Implementation

Patient Services

- **www.RigelONECARE.com** and **www.GAVRETOcopay.com** active within 2 hours of the June 24, 2024 NDA transfer
- **RigelONECARE** successfully transferred majority of Patient Assistance Program and Copay Program patients

Customer Support

- **www.GAVRETO.com** and **www.GAVRETO-hcp.com** active within 2 hours of the NDA transfer
- Patient information, dosing and administration, distribution information, and copay assistance materials deployed to the field for implementation on the day of NDA transfer

Field Team Activation

- Field team trained and ready to deliver the **GAVRETO** availability message on the day of NDA transfer
- Prioritized list of Key Accounts and prescribers contacted within the first week of availability
- Identified additional patients and prescribers

GAVRETO Q2 2024 Sales

GAVRETO is available in 2 bottle sizes

- 60 count bottle
- 90 count bottle (1.5x 60 count bottle)
- Will report 60 count equivalent bottles

228 60 ct. eq. bottles sold in Q2

(initial stocking of Rigel distribution network)

$1.9M **Q2 2024 Net Product Sales**

Clinical Development Program Update

Hematology and Oncology Pipeline Expansion

Development Opportunities[1]

Olutasidenib

- Broad range of *IDH1*-mutant cancers including AML, MDS and glioma

R289 IRAK1/4 Inhibitor

- Lower-risk MDS (LR-MDS)

Fostamatinib

- Investigator sponsored trials

Leverage Heme/Onc Capabilities

In-Licensing & Product Acquisition

- Differentiated asset(s) in hematology, oncology or related areas
- Late-stage programs
- Synergistic to current in-house capabilities and capacity

IDH1, isocitrate dehydrogenase-1, *m*IDH1, mutated IDH1; AML, acute myeloid leukemia; MDS, myelodysplastic syndrome; IRAK1/4, interleukin receptor-associated kinases 1 and 4.

1. Investigational compounds in these indications and not approved by the FDA

Strategic Alliance with MD Anderson Cancer Center to Advance Olutasidenib in AML and Other Cancers[1]

- Rigel and The University of Texas MD Anderson Cancer Center will evaluate olutasidenib in combination with other agents to treat newly-diagnosed and relapsed/refractory patients with *IDH1*-mutated:
  - ✓ AML
    - Higher-risk MDS and advanced MPN
- The collaboration will also support the evaluation of olutasidenib as:
  - Monotherapy in *IDH1*-mutated CCUS & lower-risk MDS
  - Post-transplant maintenance therapy for *IDH1*-mutated hematologic malignancies

Rigel will provide $15 million in time-based milestone payments and study material over the 5-year collaboration

AML, acute myeloid leukemia; CCUS, clonal cytopenia of undetermined significance; MDS, myelodysplastic syndrome; MPN, myeloproliferative neoplasms

1. Investigational compound in these indications and not approved by the FDA. Please see Important Safety Information on slides 45 & 46. Please visit www.REZLIDHIA.com for Full Prescribing Information, including Boxed WARNING.

Olutasidenib: Phase 1b/2 Triplet Therapy Trial in *IDH1*-mutated AML

Phase 1b/2 open-label, non-randomized clinical trial to evaluate the safety and efficacy of decitabine and venetoclax in combination with olutasidenib for m*IDH1* AML (n=78)[1]

Phase 1b: R/R m*IDH1* AML/HR-MDS

Up to 3 dose levels (6 patients per dose level) will be evaluated with:

- **Decitabine or decitabine/cedazuridine** at approved doses, days 1-5
- **Venetoclax** 400-600 mg daily, days 1-14
- **Olutasidenib** 150 mg twice daily from C1D8

RP2D

Phase 2: ND and R/R m*IDH1* AML/HR-MDS

Arm A:
Newly-diagnosed AML*
(n=30)

* Patients not eligible for intensive chemotherapy

Arm B:
R/R AML, HR-MDS
(n=30)

Key Objectives:

- Safety, tolerability and RP2D of IV/oral decitabine + venetoclax + olutasidenib
- PK

Key Objectives:

- Complete and composite remission rate (CR, CRh, CRi) and ORR
- Duration of response, EFS, OS
- MRD negativity

IDH1, isocitrate dehydrogenase-1; AML, acute myeloid leukemia: mIDH1, mutated IDH1; R/R, relapsed/refractory; HR-MDS, higher-risk myelodysplastic syndrome; RP2D, recommended Phase 2 dose; PK, pharmacokinetics; ND, newly-diagnosed; CR, complete response; CRh, CR with partial hematologic recovery; CRi, CR with incomplete recovery; ORR, overall response rate; EFS, event-free survival; OS, overall survival; MRD, minimal residual disease.

1. NCT06445959

Collaboration with CONNECT to Advance Olutasidenib in Glioma[1]

- Gliomas account for 29-35% of CNS tumors in children, adolescents and young adults; approximately 1/3 are high grade gliomas (HGG) (800-1000 new cases/year in US)[2]
- *IDH1* mutations are found in up to 36% of HGGs in adolescents and young adults[3,4,5]
- Safety and preliminary activity of single-agent olutasidenib in adult patients with relapsed/refractory high grade *IDH1*-mutant gliomas were recently reported[6]
- Olutasidenib will be included in CONNECT's TarGeT-D trial, a molecularly-guided Phase 2 umbrella clinical trial for HGG
- The Rigel-sponsored arm will evaluate a post-radiotherapy maintenance regimen of olutasidenib[1] in combination with temozolomide, followed by olutasidenib monotherapy, in newly-diagnosed adolescent and young adult patients (≤39 years) with *IDH1* mutation positive HGG

Rigel will provide funding up to $3 million and study material over the 4-year collaboration

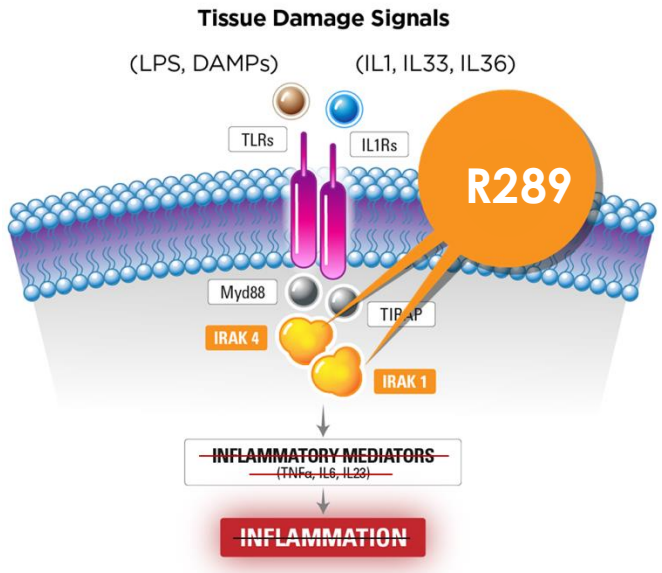
CNS, central nervous system; IDH1, isocitrate dehydrogenase-1.

1. Investigational compound in this indication and not approved by the FDA. **2.** Tejan P et al, Adolesc Health Med Ther 2017; 8. **3.** Mackay A et al. Cancer Cell. 2017; 32(4) **4.** Korshunov A et al. Acta Neuropathol. 2015; 129(5) **5.** Hartmann C et al. Acta Neuropathol. 2009; 118(4) **6.** de la Fuente MI et al. Neuro Oncol 2023; 25(1)

Targeting Inflammatory Pathways in MDS with R289, a Dual IRAK 1/4 Inhibitor[1]

Dysregulation of immune/inflammatory signaling is associated with MDS

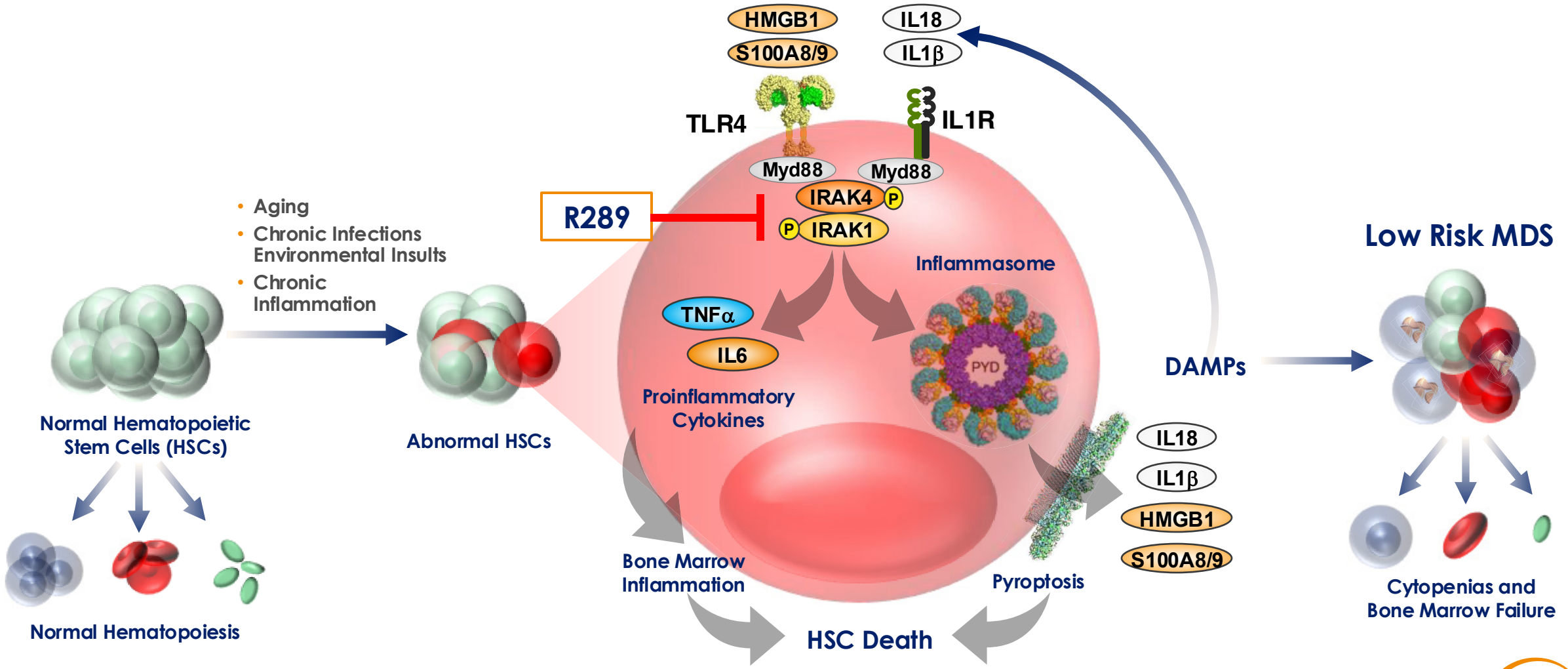
- Treatment options are limited for LR-MDS patients, especially for those with recurrent disease or who are refractory to prior lines of therapy
- IRAK 1 and 4 are key for downstream signaling of the IL-1R family and most TLRs, leading to a proinflammatory marrow environment and persistent cytopenias in patients with LR-MDS[2]
- Dual inhibition of IRAK1 & IRAK4 showed greater suppression of inflammatory cytokines vs an IRAK4-selective inhibitor *in vitro*[3]
- R835, a selective dual inhibitor of IRAK 1/4 , markedly suppressed LPS–induced cytokine release vs placebo in healthy volunteers[4]
- R289, an oral prodrug that is rapidly converted to R835 in the gut, is now being evaluated in a Phase 1b study in LR-MDS



IRAK1/4, interleukin receptor-associated kinases 1 and 4; LR, lower risk; MDS, myelodysplastic syndrome; TLR, toll-like receptor.

1. R289 is an investigational compound not approved by the FDA. **2.** Sallman DA, et al. Front Oncol. 2016;6, **3.** Lamagna C et al. Ann Rheum Dis 2020;79 (suppl 1) **4.** Yan L et al. Ann Rheum Dis 2020;79 (suppl 1)

Bone Marrow Failure in Low Risk MDS is Driven by Chronic Inflammation and Pyroptosis of Normal Hematopoietic Stem Cells[1-3]



MDS, myelodysplastic syndrome; IRAK1/4, interleukin receptor-associated kinases 1 and 4; HSC, hematopoietic stem cell; TLR, toll-like receptor; TNFα, tumor necrosis factor-α; IL, interleukin; Myd88, myeloid differentiation primary response 88; HMGB1, high mobility group box-1 protein; DAMPs, damage-associated molecular patterns.

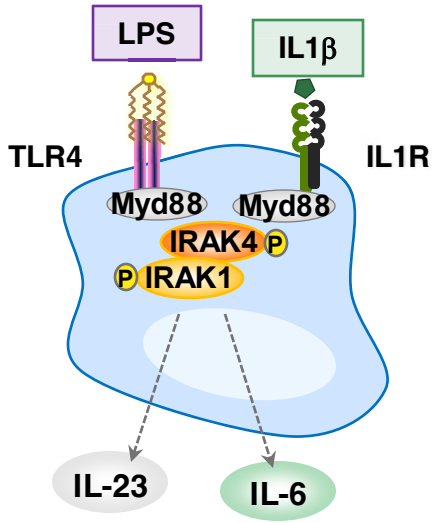
1. Sallman, DA, Front Oncol. 2016;6:151. **2.** Monlish DA, Front Immunol. 2016;7:390; **3.** Barreyro L, Blood. 2018;132(15):1553-60.

Targeting IRAK1 & IRAK4 Pathways in Inflammatory Disease

Dual Inhibition of IRAK1 and IRAK4 Provides Stronger Suppression of Inflammatory Cytokines Compared to IRAK4-selective Inhibitor[2]

Kinase Assays

Cell-Based Assays

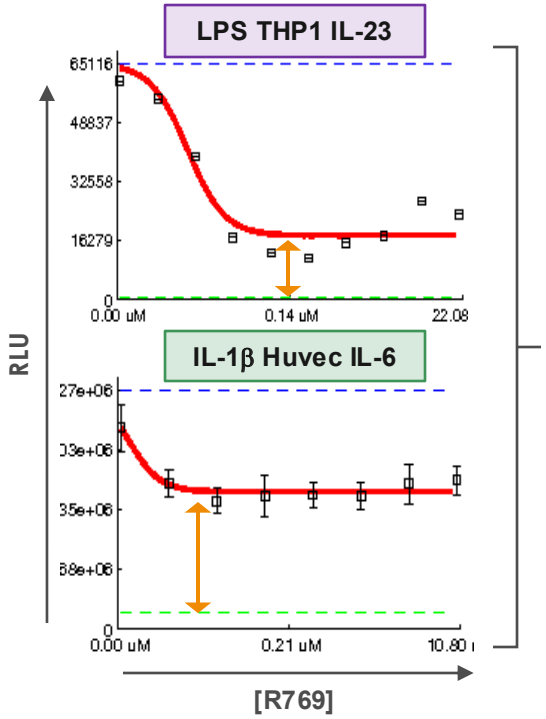


IRAK4-Selective Inhibitor

PF-06650833

IRAK4 IC_{50} = 0.2nM

IRAK1 IC_{50} = Inactive



40-80%

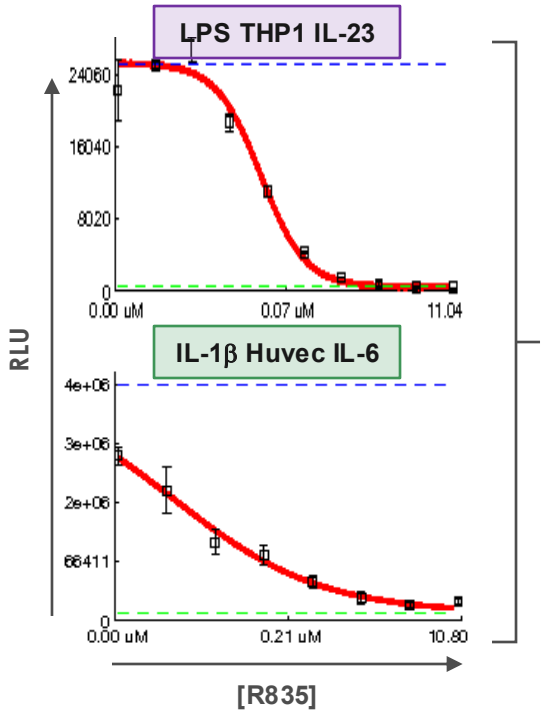
Inhibition of Cytokine Release

IRAK1/ IRAK4 Dual Inhibitor

Rigel R835[1]

IRAK4 IC_{50} = 15nM

IRAK1 IC_{50} = 14nM



100%

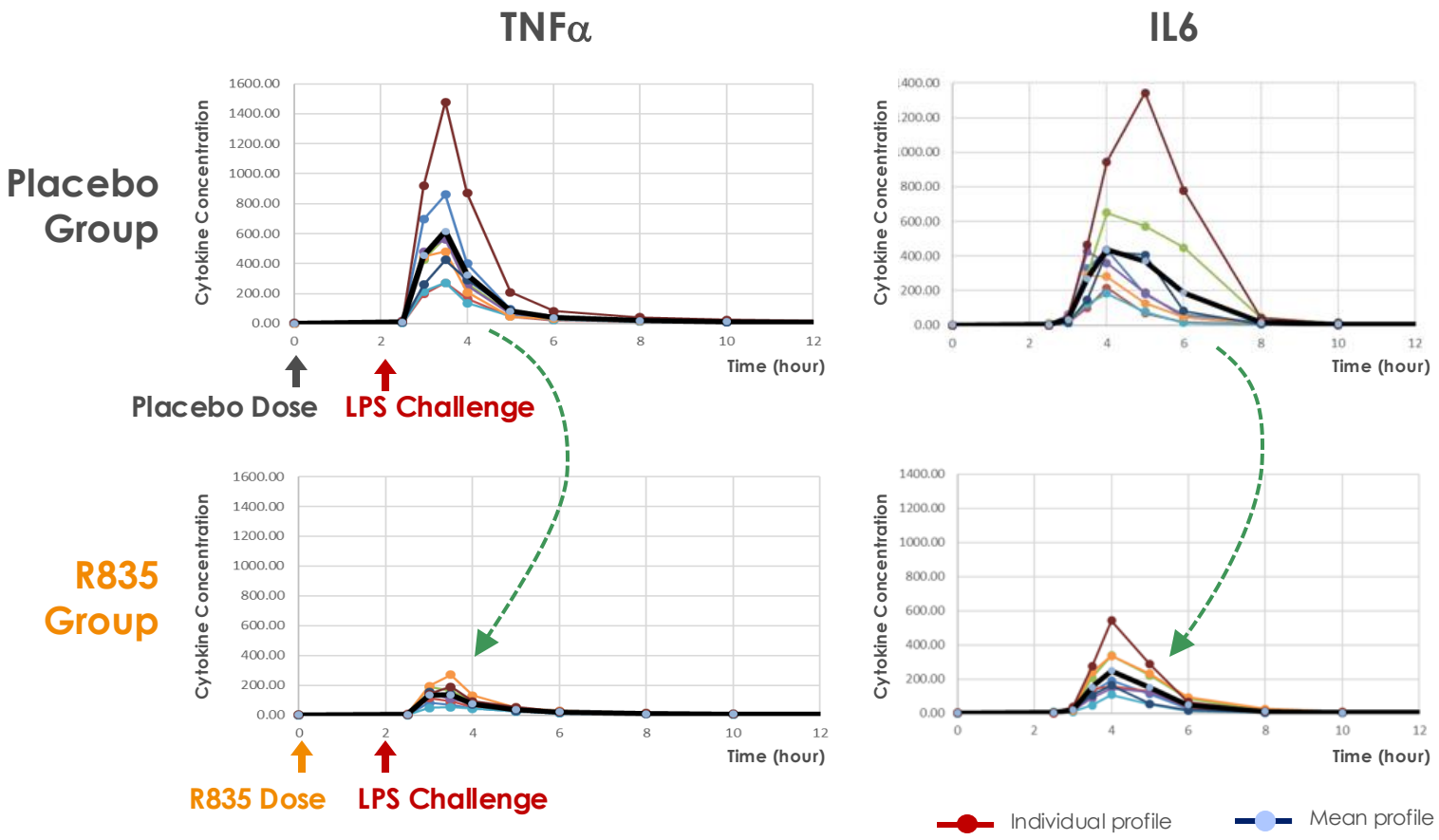
Inhibition of Cytokine Release

IRAK1/4, interleukin receptor-associated kinases 1 and 4; TLR, toll-like receptor; IL interleukin; LPS, lipopolysaccharide.

1. R835 is an investigational compound not approved by the FDA. **2.** Rigel data on file.

R835[1] Proof-of-Mechanism and First-in-Human Studies[3]

Cytokine Response After LPS Challenge



Proof-of-Mechanism

In LPS[2] Challenge study in healthy volunteers, R835 profoundly inhibited inflammatory cytokine production[2]

- Inhibited TNFα, IL-6, and IL-8

First-in-Human

First-In-Human study enrolled 82 adults to characterize the safety, PK, PD of R835

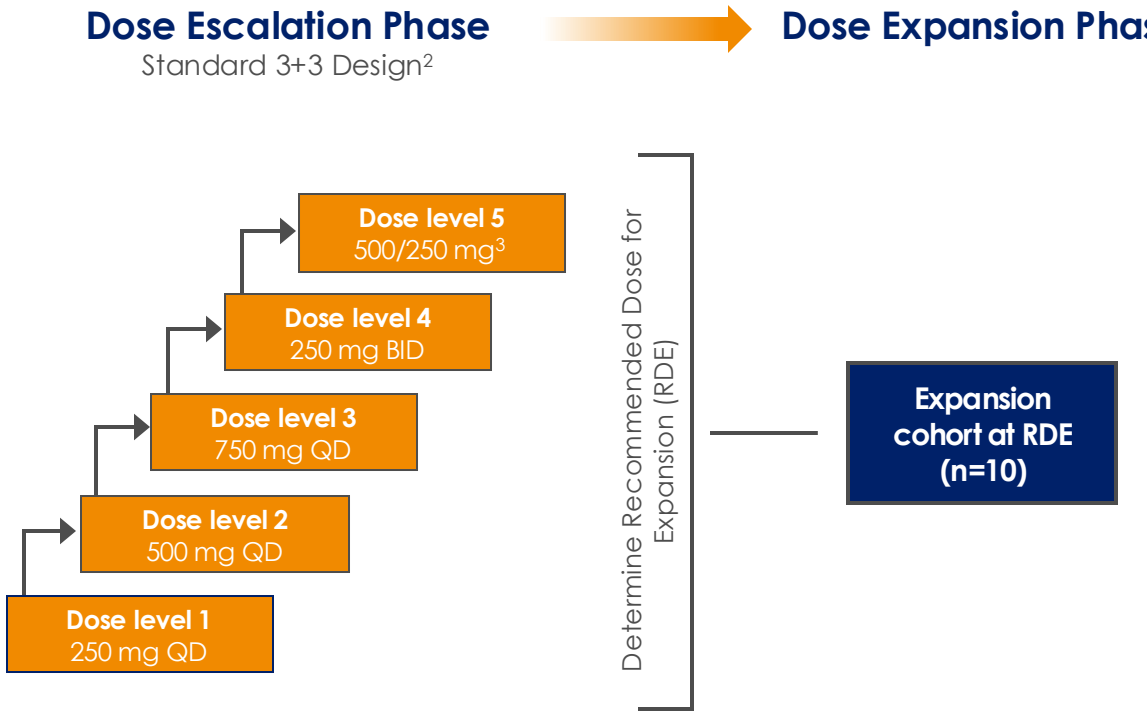
- R835 was well tolerated
- Linear PK profile and dose proportional exposure

LPS, lipopolysaccharides; TNFα, tumor necrosis factor-α; IL, interleukin; PK, pharmacokinetics; PD, pharmacodynamics; LPS, lipopolysaccharide.

1. R835 is an investigational compound not approved by the FDA. **2.** Lipopolysaccharide (LPS, a TLR4 agonist). **3.** EULAR 2020 Poster Presentation -Abstract THU0219 - First-inhuman Study of Safety, Pharmacokinetics and Pharmacodynamics of IRAK1/4 Inhibitor R835 in Healthy Subjects.

R289[1]: Phase 1b Trial in Relapsed/Refractory Lower-Risk MDS

Open-label, multicenter trial to evaluate the safety, tolerability, PK and preliminary activity of R289 in patients with LR-MDS (NCT05308264)



Primary Endpoints:

- Incidence of adverse events
- Incidence of dose-limiting toxicities

Secondary Endpoints:

- Transfusion independence
- Response rates
- Hematologic improvement
- PK
- PD

Preliminary data expected by end of 2024

MDS, myelodysplastic syndrome; QD, daily; BID, twice daily; PK, pharmacokinetics; PD, pharmacodynamics.

1. Investigational compound not approved by the FDA. **2.** Jaki T et al. *Cancer Chemother Pharmacol.* 2013; 71 **3.** Split dose: 500 mg q AM, 250 mg q PM

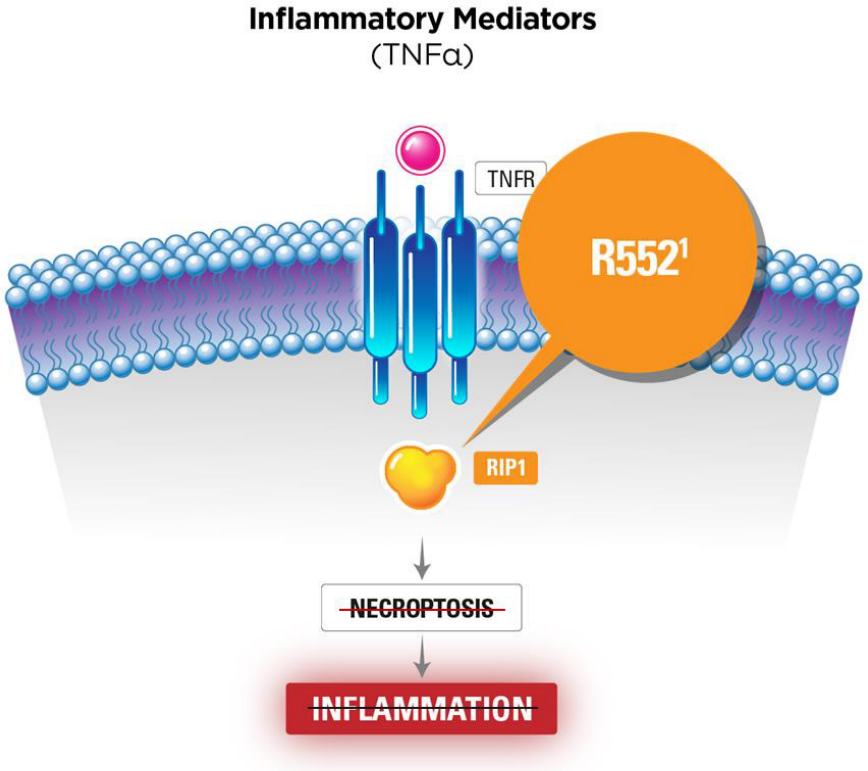
RIPK1 Inhibitor Programs in Immune and CNS Diseases with Partner Lilly

Immune Diseases

- R552, a potent and selective RIPK1 inhibitor, completed a Phase 1 study which demonstrated potential best-in-class status compared to competition
- Lilly initiated a Phase 2a clinical trial studying **ocadusertib** (previously R552 or LY3871801) in adult patients with moderately to severely active rheumatoid arthritis (RA)

CNS Diseases

- Selection of RIPK1 inhibitor candidates that cross the blood-brain barrier for CNS diseases is underway
- Lilly would lead clinical development of brain-penetrating RIPK1 inhibitors in CNS diseases



RIPK1 inhibitors play key role in TNF signaling and induction of pro-inflammatory necroptosis, which could support broad potential in RA, psoriasis and IBD, and with their experience, Lilly is the ideal partner.

RIPK1, receptor-interacting protein kinase 1; CNS, central nervous system; TNF, tumor necrosis factor; RA rheumatoid arthritis; IBD, inflammatory bowel disease.

1. Investigational compound not approved by the FDA. https://www.clinicaltrials.gov/study/NCT05848258


AI
15%
23%
62%
21324.01
12672.09
78044.32
12202.46
10212.93
32021.44
53451.08

Financials

Q2 2024 Financial Highlights

Total Revenue: $36.8M

- **Net Product Sales: $33.5M**
  - TAVALISSE: $26.4M
  - REZLIDHIA: $5.2M
  - GAVRETO: $1.9M
- **Contract Revenues from Collaborations: $3.4M**
  - Kissei $2.2M
  - Grifols $1.1M
  - Medison $0.1M

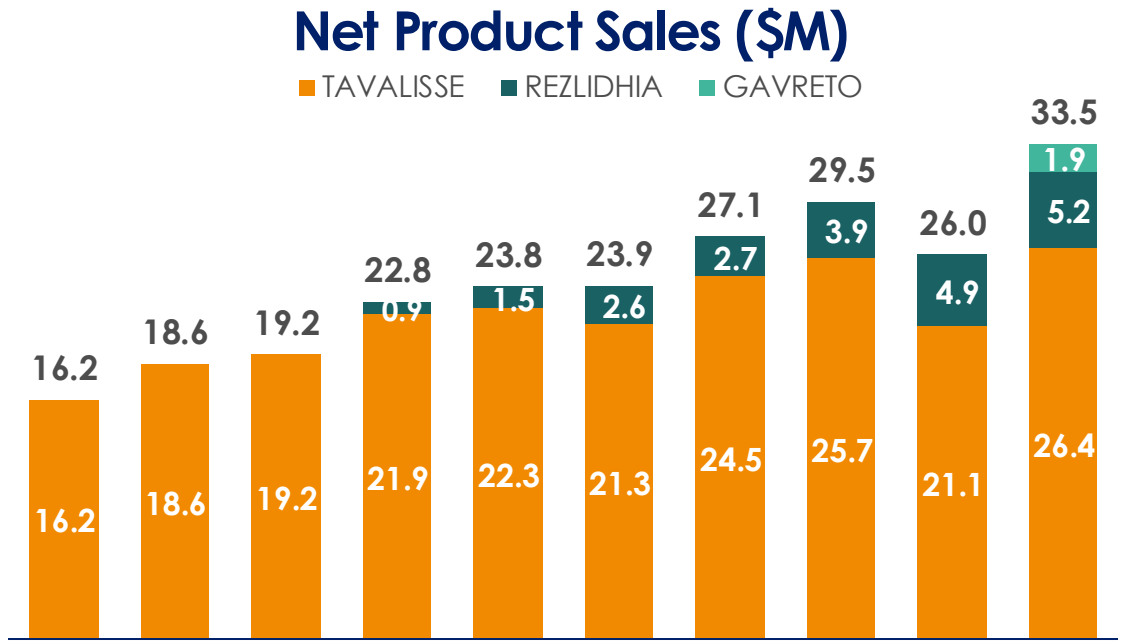
Total Bottles Shipped

- TAVALISSE: 2,722
- REZLIDHIA: 401
- GAVRETO[1]: 228

Number of Bottles Shipped to Patients and Clinics

- TAVALISSE: 2,672
- REZLIDHIA: 424
- GAVRETO[1]: n/a

Cash, Cash Equivalents & Short-Term Investments as of June 30, 2024 was $49.1M compared to $49.6M as of March 31, 2024 and $56.9 million as of December 31, 2023



		Q122	Q222	Q322	Q422	Q123	Q223	Q323	Q423	Q124	Q224
Bottles Shipped to Patients & Clinics [1]	Tavalisse	1836	2054	2026	2196	2256	2265	2412	2463	2483	2672
	Rezlidhia				2	109	187	221	278	326	424
	Gavreto										n/a
Change in Bottles in Distribution Channels	Tavalisse	-12	-1	46	221	25	-74	139	208	-290	50
	Rezlidhia				62	4	13	-11	30	64	-23
	Gavreto										228
Total Bottles Shipped	Tavalisse	1824	2053	2072	2417	2281	2191	2551	2671	2193	2722
	Rezlidhia				64	113	200	210	308	390	401
	Gavreto										228

1. GAVRETO bottle count represents 60-count bottle equivalent. 2. 1,133 total TAVALISSE bottles, net of returns; and 139 total REZLIDHIA bottles, net of returns; and 228 total GAVRETO bottles, net of returns, remained in distribution channels as of June 30, 2024.

2024 Value Drivers

Grow Product Sales for TAVALISSE, REZLIDHIA and GAVRETO

- Continue to broaden product awareness and adoption
- Identify ex-US collaboration(s) for olutasidenib

Identify In-License and Product Acquisition Opportunities

- Pursue late-stage assets which leverage current capabilities & capacity

Advance Development Programs[1]

- Enroll and generate preliminary data for R289 Phase 1b study in lower-risk MDS
- Initiate clinical trials for olutasidenib in AML, MDS, glioma and other opportunities
- Evaluate additional clinical development opportunities for olutasidenib and R289

Continue Financial Discipline

AML, acute myeloid leukemia; MDS, myelodysplastic syndrome. **1.** Investigational compounds in these indications and not approved by the FDA. Please see Important Safety Information on slides 44-48. Please visit www.TAVALISSE.com for Full Prescribing Information. Please visit www.REZLIDHIA.com for Full Prescribing Information, including Boxed WARNING. Please visit www.GAVRETO.com for Full Prescribing Information.

TAVALISSE® (fostamatinib disodium hexahydrate) Tablets

INDICATION

- TAVALISSE® (fostamatinib disodium hexahydrate) tablets is indicated for the treatment of thrombocytopenia in adult patients with chronic immune thrombocytopenia (ITP) who have had an insufficient response to a previous treatment.

IMPORTANT SAFETY INFORMATION | WARNINGS AND PRECAUTIONS

- Hypertension can occur with TAVALISSE treatment. Patients with pre-existing hypertension may be more susceptible to the hypertensive effects. Monitor blood pressure every 2 weeks until stable, then monthly, and adjust or initiate antihypertensive therapy for blood pressure control maintenance during therapy. If increased blood pressure persists, TAVALISSE interruption, reduction, or discontinuation may be required.
- Elevated liver function tests (LFTs), mainly ALT and AST, can occur with TAVALISSE. Monitor LFTs monthly during treatment. If ALT or AST increase to ≥3 x upper limit of normal, manage hepatotoxicity using TAVALISSE interruption, reduction, or discontinuation.
- Diarrhea occurred in 31% of patients and severe diarrhea occurred in 1% of patients treated with TAVALISSE. Monitor patients for the development of diarrhea and manage using supportive care measures early after the onset of symptoms. If diarrhea becomes severe (≥Grade 3), interrupt, reduce dose or discontinue TAVALISSE.
- Neutropenia occurred in 6% of patients treated with TAVALISSE; febrile neutropenia occurred in 1% of patients. Monitor the ANC monthly and for infection during treatment. Manage toxicity with TAVALISSE interruption, reduction, or discontinuation.
- TAVALISSE can cause fetal harm when administered to pregnant women. Advise pregnant women the potential risk to a fetus. Advise females of reproductive potential to use effective contraception during treatment and for at least 1 month after the last dose. Verify pregnancy status prior to initiating TAVALISSE. It is unknown if TAVALISSE or its metabolite is present in human milk. Because of the potential for serious adverse reactions in a breastfed child, advise a lactating woman not to breastfeed during TAVALISSE treatment and for at least 1 month after the last dose.

DRUG INTERACTIONS

- Concomitant use of TAVALISSE with strong CYP3A4 inhibitors increases exposure to the major active metabolite of TAVALISSE (R406), which may increase the risk of adverse reactions. Monitor for toxicities that may require a reduction in TAVALISSE dose.
- It is not recommended to use TAVALISSE with strong CYP3A4 inducers, as concomitant use reduces exposure to R406.
- Concomitant use of TAVALISSE may increase concentrations of some CYP3A4 substrate drugs and may require a dose reduction of the CYP3A4 substrate drug.
- Concomitant use of TAVALISSE may increase concentrations of BCRP substrate drugs (eg, rosuvastatin) and P-Glycoprotein (P-gp) substrate drugs (eg, digoxin), which may require a dose reduction of the BCRP and P-gp substrate drug.

ADVERSE REACTIONS

- Serious adverse drug reactions in the ITP double-blind studies were febrile neutropenia, diarrhea, pneumonia, and hypertensive crisis, which occurred in 1% of TAVALISSE patients. In addition, severe adverse reactions occurred including dyspnea and hypertension (both 2%), neutropenia, arthralgia, chest pain, diarrhea, dizziness, nephrolithiasis, pain in extremity, toothache, syncope, and hypoxia (all 1%).
- Common adverse reactions (≥5% and more common than placebo) from FIT-1 and FIT-2 included: diarrhea, hypertension, nausea, dizziness, ALT and AST increased, respiratory infection, rash, abdominal pain, fatigue, chest pain, and neutropenia.

Please see https://www.tavalisse.com/ for full Prescribing Information

To report side effects of prescription drugs to the FDA, visit http://www.fda.gov/medwatch or call 1-800-FDA-1088 (1-800-332-1088)

About REZLIDHIA® (olutasidenib)

INDICATION

REZLIDHIA is an isocitrate dehydrogenase-1 (IDH1) inhibitor indicated for the treatment of adult patients with relapsed or refractory acute myeloid leukemia (AML) with a susceptible IDH1 mutation as detected by an FDA-approved test.

IMPORTANT SAFETY INFORMATION

WARNING: DIFFERENTIATION SYNDROME

Differentiation syndrome, which can be fatal, can occur with REZLIDHIA treatment. Symptoms may include dyspnea, pulmonary infiltrates/pleuropericardial effusion, kidney injury, hypotension, fever, and weight gain. If differentiation syndrome is suspected, withhold REZLIDHIA and initiatetreatment with corticosteroids and hemodynamic monitoring until symptom resolution.

WARNINGS AND PRECAUTIONS

Differentiation Syndrome

REZLIDHIA can cause differentiation syndrome. In the clinical trial of REZLIDHIA in patients with relapsed or refractory AML, differentiation syndrome occurred in 16% of patients, with grade 3 or 4 differentiation syndrome occurring in 8% of patients treated, and fatalities in 1% of patients. Differentiation syndrome is associated with rapid proliferation and differentiation of myeloid cells and may be life-threatening or fatal. Symptoms of differentiation syndrome in patients treated with REZLIDHIA included leukocytosis, dyspnea, pulmonary infiltrates/pleuropericardial effusion, kidney injury, fever, edema, pyrexia, and weight gain. Of the 25 patients who experienced differentiation syndrome, 19 (76%) recovered after treatment or after dose interruption of REZLIDHIA. Differentiation syndrome occurred as early as 1 day and up to 18 months after REZLIDHIA initiation and has been observed with or without concomitant leukocytosis.

If differentiation syndrome is suspected, temporarily withhold REZLIDHIA and initiate systemic corticosteroids (e.g., dexamethasone 10 mg IV every 12 hours) for a minimum of 3 days and until resolution of signs and symptoms. If concomitant leukocytosis is observed, initiate treatment with hydroxyurea, as clinically indicated. Taper corticosteroids and hydroxyurea after resolution of symptoms. Differentiation syndrome may recur with premature discontinuation of corticosteroids and/or hydroxyurea treatment. Institute supportive measures and hemodynamic monitoring until improvement; withhold dose of REZLIDHIA and consider dose reduction based on recurrence.

Hepatotoxicity

REZLIDHIA can cause hepatotoxicity, presenting as increased alanine aminotransferase (ALT), increased aspartate aminotransferase (AST), increased blood alkaline phosphatase, and/or elevated bilirubin. Of 153 patients with relapsed or refractory AML who received REZLIDHIA, hepatotoxicity occurred in 23% of patients; 13% experienced grade 3 or 4 hepatotoxicity. One patient treated with REZLIDHIA in combination with azacitidine in the clinical trial, a combination for which REZLIDHIA is not indicated, died from complications of drug-induced liver injury. The median time to onset of hepatotoxicity in patients with relapsed or refractory AML treated with REZLIDHIA was 1.2 months (range: 1 day to 17.5 months) after REZLIDHIA initiation, and the median time to resolution was 12 days (range: 1 day to 17 months). The most common hepatotoxicities were elevations of ALT, AST, blood alkaline phosphatase, and blood bilirubin

IMPORTANT SAFETY INFORMATION (Cont.)

WARNINGS AND PRECAUTIONS

Hepatotoxicity

Monitor patients frequently for clinical symptoms of hepatic dysfunction such as fatigue, anorexia, right upper abdominal discomfort, dark urine, or jaundice. Obtain baseline liver function tests prior to initiation of REZLIDHIA, at least once weekly for the first two months, once every other week for the third month, once in the fourth month, and once every other month for the duration of therapy. If hepatic dysfunction occurs, withhold, reduce, or permanently discontinue REZLIDHIA based on recurrence/severity.

ADVERSE REACTIONS

The most common (≥20%) adverse reactions, including laboratory abnormalities, were aspartate aminotransferase increased, alanine aminotransferase increased, potassium decreased, sodium decreased, alkaline phosphatase increased, nausea, creatinine increased, fatigue/malaise, arthralgia, constipation, lymphocytes increased, bilirubin increased, leukocytosis, uric acid increased, dyspnea, pyrexia, rash, lipase increased, mucositis, diarrhea and transaminitis.

DRUG INTERACTIONS

- Avoid concomitant use of REZLIDHIA with strong or moderate CYP3A inducers.
- Avoid concomitant use of REZLIDHIA with sensitive CYP3A substrates unless otherwise instructed in the substrates prescribing information. If concomitant use is unavoidable, monitor patients for loss of therapeutic effect of these drugs.

LACTATION

Advise women not to breastfeed during treatment with REZLIDHIA and for 2 weeks after the last dose.

GERIATRIC USE

No overall differences in effectiveness were observed between patients 65 years and older and younger patients. Compared to patients younger than 65 years of age, an increase in incidence of hepatotoxicity and hypertension was observed in patients ≥65 years of age.

HEPATIC IMPAIRMENT

In patients with mild or moderate hepatic impairment, closely monitor for increased probability of differentiation syndrome.

You may report side effects to the FDA at 1-800-FDA-1088 or www.fda.gov/medwatch.

Please see https://www.REZLIDHIA.com/ for full Prescribing Information, including Boxed WARNING.

About GAVRETO® (pralsetinib)

INDICATIONS

GAVRETO (pralsetinib) is indicated for the treatment of:

- Adult patients with metastatic rearranged during transfection (RET) fusion-positive non-small cell lung cancer (NSCLC) as detected by an FDA-approved test
- Adult and pediatric patients 12 years of age and older with advanced or metastatic RET fusion-positive thyroid cancer who require systemic therapy and who are radioactive iodine-refractory (if radioactive iodine is appropriate)*

*This indication is approved under accelerated approval based on overall response rate and duration of response. Continued approval for this indication may be contingent upon verification and description of clinical benefit in confirmatory trial(s).

IMPORTANT SAFETY INFORMATION

- **Interstitial Lung Disease (ILD)/Pneumonitis:** Severe, life-threatening, and fatal ILD/pneumonitis can occur in patients treated with GAVRETO. Pneumonitis occurred in 12% of patients who received GAVRETO, including 3.3% with Grade 3-4, and 0.2% with fatal reactions. Monitor for pulmonary symptoms indicative of ILD/pneumonitis. Withhold GAVRETO and promptly investigate for ILD in any patient who presents with acute or worsening of respiratory symptoms (e.g., dyspnea, cough, and fever). Withhold, reduce dose or permanently discontinue GAVRETO based on severity of confirmed ILD.

- **Hypertension:** Occurred in 35% of patients, including Grade 3 hypertension in 18% of patients. Overall, 8% had their dose interrupted and 4.8% had their dose reduced for hypertension. Treatment-emergent hypertension was most commonly managed with anti-hypertension medications. Do not initiate GAVRETO in patients with uncontrolled hypertension. Optimize blood pressure prior to initiating GAVRETO. Monitor blood pressure after 1 week, at least monthly thereafter and as clinically indicated. Initiate or adjust anti-hypertensive therapy as appropriate. Withhold, reduce dose, or permanently discontinue GAVRETO based on the severity.

- **Hepatotoxicity:** Serious hepatic adverse reactions occurred in 1.5% of patients treated with GAVRETO. Increased aspartate aminotransferase (AST) occurred in 49% of patients, including Grade 3 or 4 in 7% and increased alanine aminotransferase (ALT) occurred in 37% of patients, including Grade 3 or 4 in 4.8%. The median time to first onset for increased AST was 15 days (range: 5 days to 2.5 years) and increased ALT was 24 days (range: 7 days to 3.7 years). Monitor AST and ALT prior to initiating GAVRETO, every 2 weeks during the first 3 months, then monthly thereafter and as clinically indicated. Withhold, reduce dose or permanently discontinue GAVRETO based on severity.

- **Hemorrhagic Events:** Serious, including fatal, hemorrhagic events can occur with GAVRETO. Grade ≥3 events occurred in 4.1% of patients treated with GAVRETO including one patient with a fatal hemorrhagic event. Permanently discontinue GAVRETO in patients with severe or life-threatening hemorrhage.

- **Tumor Lysis Syndrome (TLS):** Cases of TLS have been reported in patients with medullary thyroid carcinoma receiving GAVRETO. Patients may be at risk of TLS if they have rapidly growing tumors, a high tumor burden, renal dysfunction, or dehydration. Closely monitor patients at risk, consider appropriate prophylaxis including hydration, and treat as clinically indicated.

IMPORTANT SAFETY INFORMATION (Cont.)

- **Risk of Impaired Wound Healing:** Impaired wound healing can occur in patients who receive drugs that inhibit the vascular endothelial growth factor (VEGF) signaling pathway. Therefore, GAVRETO has the potential to adversely affect wound healing. Withhold GAVRETO for at least 5 days prior to elective surgery. Do not administer for at least 2 weeks following major surgery and until adequate wound healing. The safety of resumption of GAVRETO after resolution of wound healing complications has not been established.

- **Embryo-Fetal Toxicity:** Based on findings from animal studies and its mechanism of action, GAVRETO can cause fetal harm when administered to a pregnant woman. Advise pregnant women of the potential risk to a fetus. Advise females of reproductive potential to use effective non-hormonal contraception during treatment with GAVRETO and for 2 weeks after the last dose. Advise males with female partners of reproductive potential to use effective contraception during treatment with GAVRETO and for 1 week after the last dose.

- **Common adverse reactions (≥25%)** were musculoskeletal pain, constipation, hypertension, diarrhea, fatigue, edema, pyrexia, and cough. **Common Grade 3/4 laboratory abnormalities (≥2%)** were decreased lymphocytes, decreased neutrophils, decreased hemoglobin, decreased phosphate, decreased leukocytes, decreased sodium, increased aspartate aminotransferase (AST), increased alanine aminotransferase (ALT), decreased calcium (corrected), decreased platelets, increased alkaline phosphatase, increased potassium, decreased potassium, and increased bilirubin.

- Avoid coadministration of GAVRETO with **strong or moderate CYP3A inhibitors, P-gp inhibitors, or combined P-gp and strong or moderate CYP3A inhibitors.** If coadministration cannot be avoided, reduce the GAVRETO dose. Avoid coadministration of GAVRETO with **strong or moderate CYP3A inducers**. If coadministration cannot be avoided, increase the GAVRETO dose.

- **Lactation:** Advise women not to breastfeed during treatment with GAVRETO and for 1 week after the last dose.

- **Pediatric Use:** Monitor open growth plates in adolescent patients. Consider interrupting or discontinuing GAVRETO if abnormalities occur.

You may report side effects to the FDA at 1-800-FDA-1088 or www.fda.gov/medwatch.

Please see https://www.GAVRETO.com/ for full Prescribing Information.

Thank You

www.rigel.com